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# Synthesis, Characterisation and Antimicrobial Activity of Novel Phosphine Stablised Silver (1) Dicarboxylate Complexes

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# SYNTHESIS, CHARACTERISATION AND ANTIMICROBIAL ACTIVITY OF NOVEL PHOSPHINE STABLISED SILVER (I) DICARBOXYLATE COMPLEXES

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**DOCTOR OF PHILOSOPHY**

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## ABSTRACT

The α, ω-dicarboxylic acids HOOC-$(CH_2)_n$-COOH (where n = 1-11) reacted smoothly with [$Ag(CH_3COO)$] to yield 11 novel silver dicarboxylate complexes. These silver dicarboxylates were reacted with triphenylphosphine ($PPh_3$) in 1:2.5, 1:4 and 1:6 molar ratios resulting in the isolation of 30 novel silver dicarboxylate triphenylphosphine derivatives. X-ray crystal structures for nine of these complexes were determined showing a variation in the structural motifs across the series with mononuclear, dinuclear, polynuclear and polymeric species being generated. When the 11 novel silver dicarboxylate complexes were reacted with bis-(diphenylphosphino)methane (dppm) in a 1:2 molar ratio 11 novel complexes were isolated. The complexes were isolated as powders and 8 of them formulated as [$Ag_2$(dicarboxylate)$(dppm)_4$] with the remainder having just three dppm ligands in their formulae. The only crystals isolated from this series precipitated from the mother liquor of the reaction involving dodecanedicarboxylic acid ($dddaH_2$), which formulated as $\{Ag_2(dppm)_2(ddda)(H_2O)\}_n$ and whose structure comprises a linear polymer in which centrosymmetric $Ag_2(dppm)_2$ units are linked by diacid anions.

The 11 novel silver dicarboxylate complexes were reacted with bis-(diphenylphosphino)ethane (dppe) in a 1:2 molar ratio using the same procedure employed for the dppm reactions to yield 11 novel complexes which again were isolated as powders and formulated as either [$Ag_2$(dicarboxylate)$(dppe)_4$] or [$Ag_2$(dicarboxylate)$(dppe)_3$]. All of the complexes were found to have limited solubilities and the phosphine derivatives were all relatively light stable compared to simple silver salts such as $AgNO_3$.

The metal free dicarboxylic acids and phosphine based ligands are relatively poor antifungals and display no antibacterial activity. The 11 silver dicarboxylate complexes are potent in-vitro anti-*Candida* agents but only five of them displayed good antibacterial activity, although it was significantly less than that of $AgNO_3$. Furthermore, unlike the activity of $AgNO_3$ these five complexes displayed some discrimination towards the Grampositive (*S. aureus* /MRSA) and Gramnegative (*E.coli*) bacteria suggesting that these complexes do not act on microbial cells in the same way as $AgNO_3$. All of the $PPh_3$ complexes exhibited significant antifungal activity against

the *Candida albicans* cells although their activity is, on average, over ten times less than that of the equivalent silver dicarboxylate. Only 5 of these complexes are active against the bacterial cells tested. Three of these complexes display higher antibacterial activity (comparable to that of $AgNO_3$) than antifungal activity, a trend not previously observed. The dppm and dppe derivatives all exhibited significant antifungal activity against the *Candida albicans* cells. However, most of their activities are again significantly less than that of the equivalent silver dicarboxylate. Only three of these complexes display any activity against the bacterial cells tested and one of them exhibits good activity against the Grampositive MRSA but it is inactive against the Gramnegative *E.coli.*

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## SYMBOLS AND ABBREVIATIONS

| | |
|---|---|
| $PPh_3$ | Triphenylphosphine |
| $prdaH_2$ | Propanedioic acid |
| $bdaH_2$ | Butanedioic acid |
| $pdaH_2$ | Pentanedioic acid |
| $hxdaH_2$ | Hexanedioic acid |
| $hdaH_2$ | Heptanedioic acid |
| $odaH_2$ | Octanedioic acid |
| $ndaH_2$ | Nonanedioic acid |
| $ddaH_2$ | Decanedioic acid |
| $uddaH_2$ | Undecondioic acid |
| $dddaH_2$ | Dodecanedioic acid |
| $uddcaH_2$ | Undecondicaboxylic acid |
| ν | Wavenumber |
| ° | Degrees |
| °C | Degrees Celsius |
| DMSO | Dimethylsulphoxide |
| IR | Infrared |
| Sym | Symmetric |
| Asym | Asymmetric |
| α | Alpha |
| $IC_{50}$ | Drug concentration eliciting 50% of max. inhibition |
| *ca.* | Circa |
| 14DM | 14α-demethylase |
| DNA | Deoxyribosenucleic acid |
| PBS | Phosphate buffer saline |
| RNA | Ribonucleic acid |
| RPMI | Roswell Park Memorial Institute |
| SDA | Sabouraud dextrose agar |
| Å | Angstrom |
| EtOH | Ethanol |
| H, min, s | Hours, minutes, seconds |

| | |
|---|---|
| K | Kelvin |
| MeOH | Methanol |
| R | Alkyl, aryl, aromatic substituent |
| Hasp | Acetasalicyclic acid |

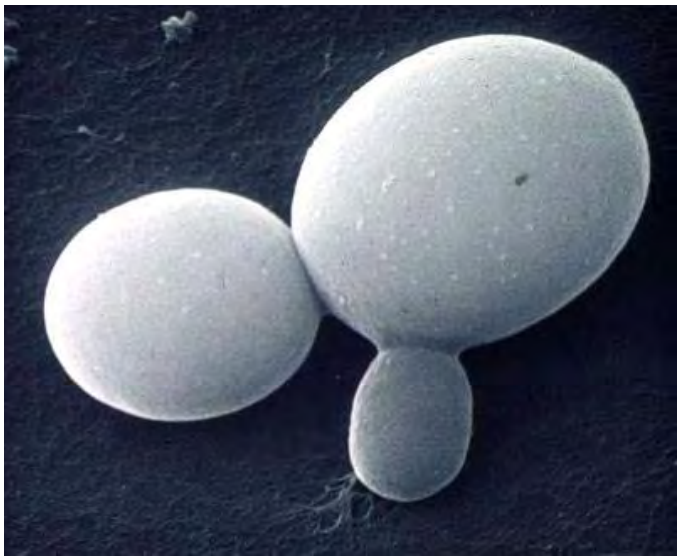
# INTRODUCTION

## I General Introduction

During the last two decades the frequency and types of life-threatening fungal and bacterial infections has increased dramatically. This has been as a result of changes in both medical practice and in the diseases to which humans are exposed. The yeast *Candida albicans*, is considered to be the most opportunistic fungal pathogen as it presents itself in immunocompromised patients, and over 75% of women suffer from vaginal candidosis at some stage in their lifetime. *Candida* infections are diverse in their manifestations, varying from superficial skin problems, chronic infection of the nails, mouth, throat or vagina to frequently fatal systemic diseases that involve the lungs, heart, gastrointestinal tract, central nervous system and other organs. These infections are considered to be opportunistic in nature since some aspect of the host's defence system is impaired in some way. *C. albicans* is a dimorphic yeast, existing in a yeast phase (blastospore) and having the ability to form germ tubes that elongate into hyphae (hyphal phase). The definitions of the two phases are given below.

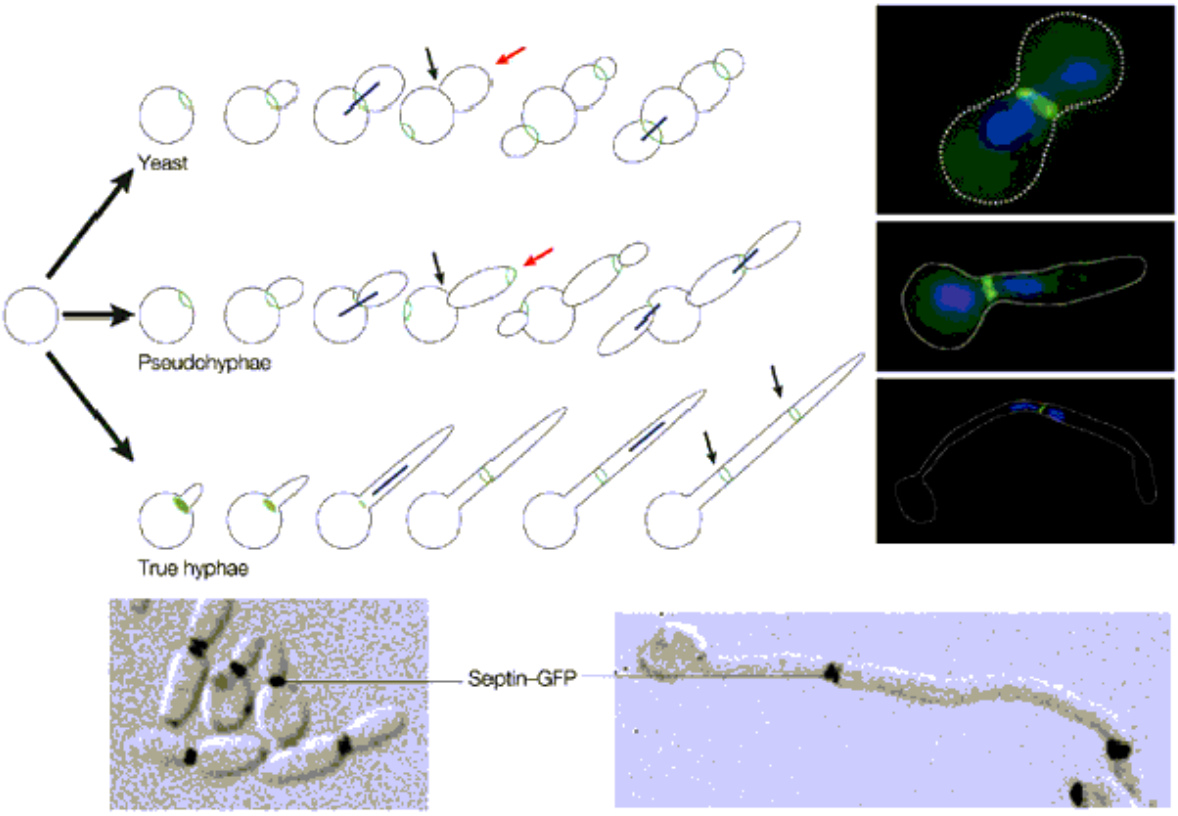
A blastospore is defined as the unicellular form of the fungus, the yeast cell.It is distinguished by a specific process of mitotic cell division known as budding (Figure 1). Budding involves the growth of new cellular material from selected sites on the blastospore surface. The new bud grows for a period of time until it is one third the size of the parent blastospore, and then stops. Nuclear division follows and a septum is laid down between the parent and the daughter cell. The two cell units separate and form two blastospores. [1]

***Figure 1:*** A yeast cell budding[2]



In mycology, germination refers to a process in which a hardy dominant spore undergoes a complex set of metabolic rearrangements and cell wall alterations to generate a new hyphal cell. This cell emerges through a pore in the wall of the spore as a germ tube of different molecular architecture from the spore. This nomenclature is being used in all studies of *C. albicans* to define a process where a novel hypha emerges by a simple evagination of the cell wall. Septae are laid down along the extending hyphae. The term "germ tube" is used to refer to newly evaginating hypha up to the time that the first septum is laid down.

***Figure 2***: Yeast cells, pseudohyphal cells and true hyphal cells[3]




*Candida albicans* can exist in three forms that have distinct shapes: yeast cells (also known as blastospores), pseudohyphal cells and true hyphal cells (Figure 2). Yeast cells are round to ovoid in shape and separate readily from each other. Pseudohyphae resemble elongated, ellipsoid yeast cells that remain attached to one another at the constricted septation site and usually grow in a branching pattern that is thought to facilitate foraging for nutrients away from the parental cell and colony. True hyphal cells are long and highly polarized, with parallel sides and no obvious constrictions

between cells. All three cell types have a single nucleus per cell before mitosis. Important differences between yeast, pseudohyphal and true hyphal cells include the degree of polarized growth, the positioning of the septin ring (green in Figure 2 and micrographs, and black in light microscope images) and of the true septum relative to the mother cell, the movement of the nucleus (blue line in Figure 2 and in micrographs) relative to the mother cell and the degree to which daughter cells are able to separate into individuals.

Many of the current antifungal agents that are used in therapy are generating resistance or have adverse side effects. For example, the anti-*Candida* agent, fluconazole can cause nausea, headache or provoke liver damage. As a result of this increase in resistance, infections caused by other *Candida* species such as *Candida glabrata, Candida kreusi* and *Candida dublineinsis* are becoming more common.

Antibacterial drug discovery reached its apex in the 1950's and of the majority of these compound classes are still in use today.[4] After the introduction of streptogramins and quinolones in the early 1960's, no novel class of antibacterial agent was introduced into clinical practice until linezolid was launched in 2000. Due to the diversity of bacterial structures, drug discovery in this area requires agents with specific biomolecular targets or pathways. Bacterial microorganisms have made use of antibacterial xenobiotics and selective pressure to evolve an elaborate arsenal of defences to protect themselves from attack. As a result, some researchers suggest the superior role of natural products, due to evolutionary conditions, in producing an array of antibiotic producing microorganism, compared with synthetic libraries.[5] However, these antibiotics function by targeting specific biomolecular pathways and as a result have a propensity for the development of resistance to prophylactic treatment.

The major types of bacterial organisms which cause community and hospital acquired infections are (i) Methicillin-resistant *Staphylococcus aureus* (MRSA), (ii) *Clostridium-difficile* (*C.difficile*) and (iii) *Escherichia-coli (E-Coli*).

**Methicillin-resistant *Staphylococcus aureus* (MRSA)**

MRSA has been pandemic for over a decade and is causing a major increase in serious staphylococcal infections.[6] It is a variety of S*taphylococcus aureus* (SA) which exists on the skin and nose of about 30% of the population without causing any serious health effects but can cause wound infections and severe bloodstream infections.[7] Penicillin was introduced in 1940 to fight against these infections but within a short period of time nearly all strains of SA became resistant to it. Methicillin was then introduced to overcome this resisitance but about 60% of SA strains have now become resistant to it. The antibiotic drug vancomycin, is currently used to treat these infections but it is not effective and resistance to this drug is also beginning to emerge.[8]

***Clostridium-difficile* (*C.difficile*)**

*Clostridium difficile* (*C.difficile*) is an anaerobic bacterium which is usually found in the large intestine and it can be found in a small portion of healthy adult population. It is traditionally a nosocomial pathogen and is one of the leading causes of diarrhoea. It usually occurs in patients that have had their natural intestinal bacteria destroyed by antibiotics. In the absence of normal bacteria it multiplies and produces toxins that damage the lining of the intestine resulting in diarrhoea.[9] *C.difficile* spores can persist in dust or on surfaces for months and can be transmitted to other patients or to healthcare workers. The spores cannot be destroyed by usual detergents and survive hand disinfections with alcoholic preparations. Therefore it is important to try and establish an effective strategy for controlling the spread of this infection.[10]

***Escherichia-coli (E-Coli*)**

*Escherichia-coli (E-Coli*) is an anaerobic Gramnegative bacterium that is found in the intestinal tracts of healthy animals.[11] It can adhere to the mucus overlying the large intestine and once established it can persist there for months or years. It becomes problematic for a patient if the natural flora in the gut is disturbed particularly after a course of antimicrobial chemotherapy.[12] It is one of the leading causes of urinary tract infections and can form biofilms on catheters.

## I.1 GENERAL CHEMISTRY OF SILVER

Silver is a white metal, more malleable and ductile than other metal except gold. Silver, one of the "coinage metals" was almost certainly one of the first three metals known to man along with the other "coinage metals", gold and copper. It has been known and valued as an ornamental and coinage metal since ancient times and silver mines in Asia Minor were probably worked before 2500 BC. The alchemists called the metal Luna or Diana after the goddess of the moon and ascribed to it the symbol of a crescent moon. It's principle ore is argentite or "horn Silver". Silver has the electron configuration [Kr] $4d^{10}$ $5s^{1}$. Its hardness ranges between 2.5 and 2.7; it is harder than gold but softer than copper. Silver melts at about 962 °C, boils at about 2212° C and has a specific gravity of 10.5. The atomic weight of silver is 107.868 g $mol^{-1}$.

### I.1.1 The silver(I) oxidation state

Ag(I) is by far the most important oxidation state and is the most commonly known, with the electron configuration [Kr] $4d^{10}$. $Ag^{+}$ forms a large variety of complexes. Most simple ligands have a coordination number of two e.g. the silverdiammine complex $[Ag(NH_3)_2]^{+}$, $[Ag(CN)_2]^{-}$ and $[Ag(S_2O_3)_2]^{3-}$ and are therefore linear in shape. However complexes of coordination number three, four and six are also found, with trigonal, planar, square planar, tetrahedral and octahedral structures commonly seen. Ligands capable of $\pi$ bonding, such as phosphine derivatives, may form both two- and four-coordinate complexes. A few silver(I) complexes with colourless anions are coloured. AgI, $Ag_2CO_3$ and $Ag_3PO_4$ are yellow and $Ag_2S$ is black. This is due to the small and highly polarising silver(I) ion and the anion, eg. $I^{-}$, being large and highly polarisable. This leads to some covalent character.

### I.1.2 The silver(II) oxidation state

The silver(II) ion has the electron configuration [Kr] $4d^{9}$. Numerous complexes of Ag(II) are known, and are usually prepared by oxidizing a solution of silver(I) containing the complexing ligand with potassium persulphate. These complexes are usually square planar and paramagnetic. With neutral ligands cationic species such as $[Ag(pyridine)_4]^{2+}$, $[Ag(bipyridine)_2]^{2+}$ and $[Ag(\textit{ortho}\text{- phenanthroline})_2]^{2+}$ form crystalline salts. The magnetic moments of Ag(II) complexes range from $\mu_{eff}$ =1.75 to 2.2 BM, consistent with a $d^{9}$ configuration.

### I.1.3 The silver(III) oxidation state

The silver(III) oxidation state is very uncommon. The flourination of a fused mixture of alkali metal halide and silver halide will give $M^{+}[Ag^{III}F_4]^{-}$, and the electrolytic oxidation of silver(I) can give impure $Ag_2O_3$. Oxidation of alkaline $Ag_2O$ with persulphate gives mixed oxide $Ag^{I}Ag^{II}O_2$. Persulphate in the presence of periodate or tellurate ions gives compounds such as $K_6H[Ag^{III}(IO_6)_2]$ and $Na_6H[Ag^{III}(TeO_6)_2]$. These compounds are all unstable and are strong oxidising agents.

### I.1.4 Complexes of silver(I)

#### I.1.4.1 Silver(I) and its coordination modes

Silver(I) has an outer electron configuration of $[Kr]d^{10}$ and is diamagnetic. It forms good complexes with nitrogen, sulphur and halogen donor ligands. Silver(I) has a low affinity for oxygen donors although complexes containing carboxylate ions and crown ethers are known. Numerous phosphine complexes of silver(I) are also known. There are a number of coordination modes and geometries of silver(I) complexes. The most common are linear (coordination number 2), trigonal planar (coordination number 3), tetrahedral (coordination number 4) and octahedral (coordination number 6).[13] Examples of these are shown in Figure 3.

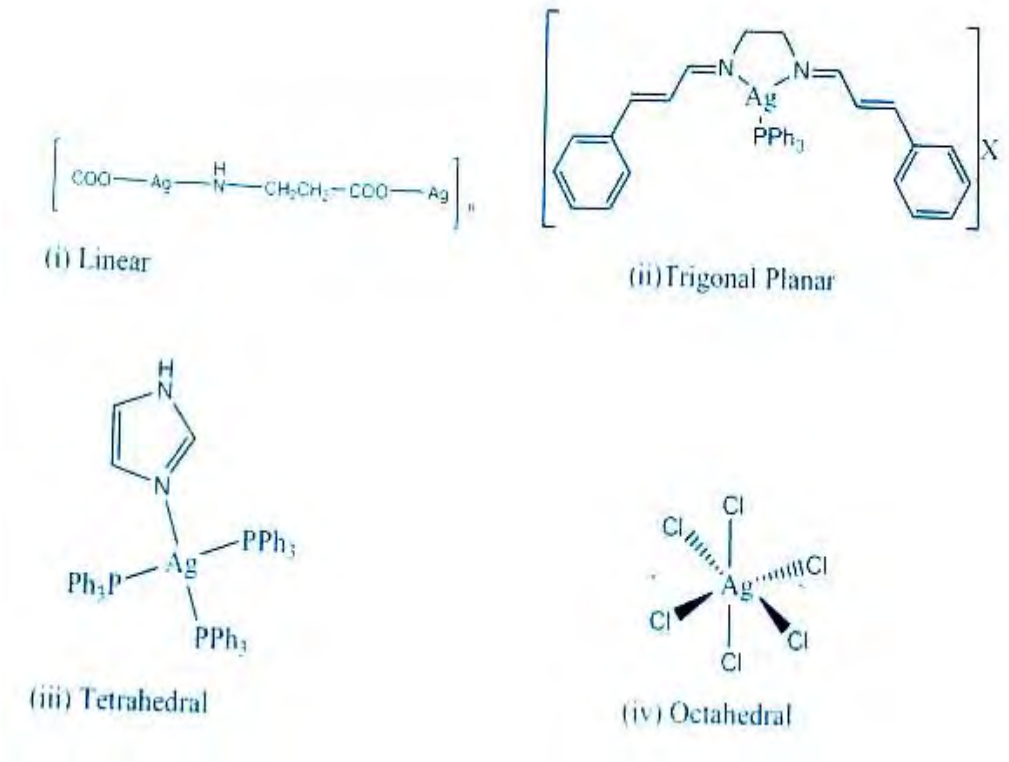



***Figure 3***: Structures of the most common coordination modes and geometries of silver(I): (i) linear, (ii) trigonal planar, (iii) tetrahedral and (iv) octahederal[13]

### I.1.4.2 Complexes with Nitrogen Ligands

Many of the silver complexes with nitrogen ligands readily form in aqueous solution. [13] $NH_3$ is most important of the nitrogen ligands. There is a preference for linear coordination, the linear $[H_3N\text{-}Ag\text{-}NH_3]^+$ ion has been observed crystallographically in several compounds. Formation of this ion is dependent on $[Ag^+]$ and $[NH_3]$, it can be used for the separation of silverhalides.The solubility of AgCl gives $[Ag(NH_3)_2]Cl$ on treatment with aqueous ammonium carbonate, while AgBr dissolves only in aqueous ammonia, in which AgI is poorly soluble.

Aqueous pyridine and substituted pyridines form $[Ag(py)_2]^+$ and $[Ag(py)_2]^+$ ions, but in non-aqueous conditions tetrahedral complexes, such as $[Ag(py)_4]ClO_4$, may be obtained. The tetrahedral acetonitrile adduct $[Ag(NCMe)_4]^+$ is also known and is quite stable. There are a number of argentite(I) complexes such as $[Ag(NCO)_2]^-$ and

$[Ag(ONO_2)_2]^-$; they are linear, with 2-coordinate $Ag^+$. Linear coordination is also found in the tetrameric silver amide $[Ag\{N(SiMe_3)_2\}]_4$.

### I.1.4.3 Complexes with Halogen Ligands

The halides AgX react with halide anions $X^-$ (where X is $I^- > Br^- > Cl^-$) to give a series of anionic complexes $[Ag_KX_l]^{(l-K)-}$, with relative stabilities $I^- > Br^- > Cl^-$.[13] The type of complex anion formed is strongly influenced by the counterion and the nature of the halide, and there is considerable structural diversity. The ions $[X\text{-}Ag\text{-}X]^-$ (X = Cl, Br) are linear, where as $[Ag_2X_4]^{2-}$(X = Cl, Br, I) and $[AgI_3]^-$ contain 3-coordinate silver. Examples of anionic iodo complexes are shown in Figure 4. Cationic species such as $Ag_2X^+$ and $Ag_3X_2^+$ are formed when the silver halides are dissolved in aqueous solution of $AgNO_3$ and $AgClO_4$.

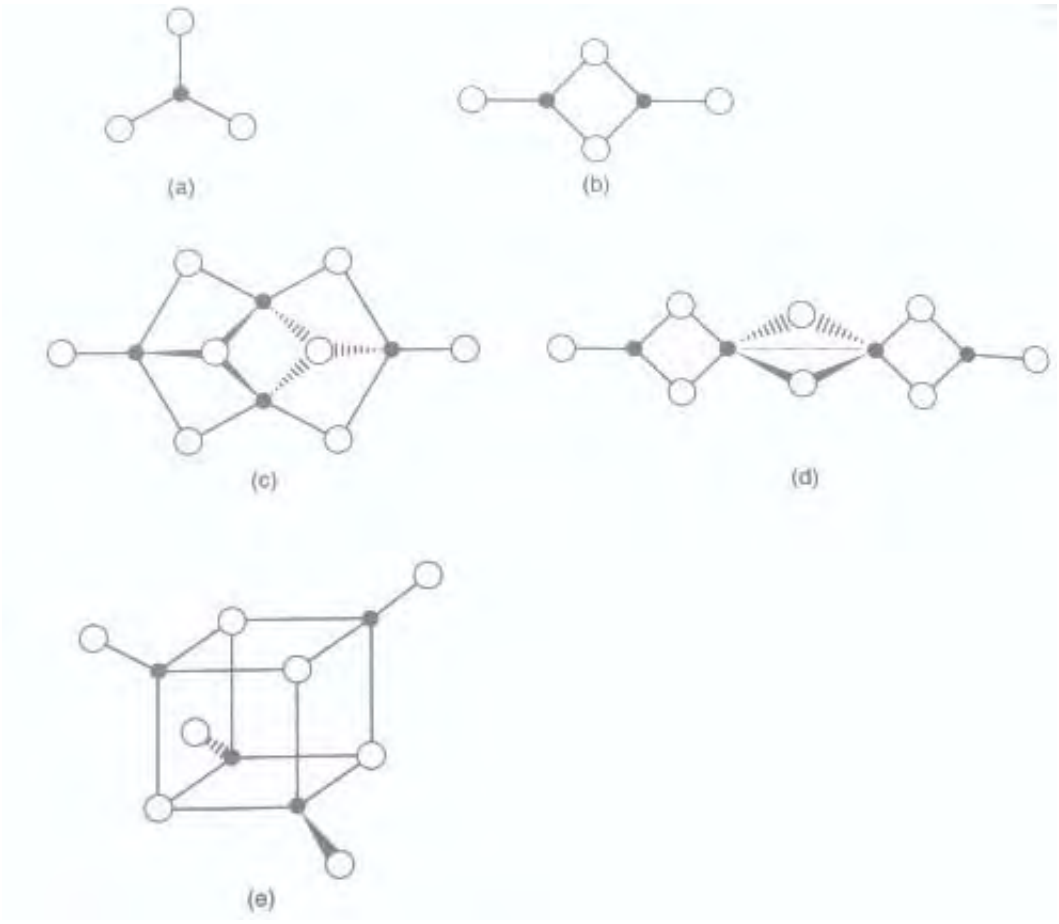



***Figure 4***: Structures of the anionic iodoargentate complexes (a) $[AgI_3]^{2-}$; (b) $[Ag_2I_4]^{2-}$; (c)-(e) isomers of $[Ag_4I_8]^{4-}$ [13]

### I.1.4.4 Complexes with Phosphine Ligands

With monophosphines these are mainly of the type $(R_3P)_n$ AgX, with n=1-4.[14] The 1:1 complexes are tetrameric, with either cubane figure or chair figure structures depending on the steric requirements of both X and $R_3P$; $Ag_4I_4(PPh_3)_4$ undergoes cube-chair isomerisation, and the two structural types may be obtained by crystallization from different solvents (Figure 5).

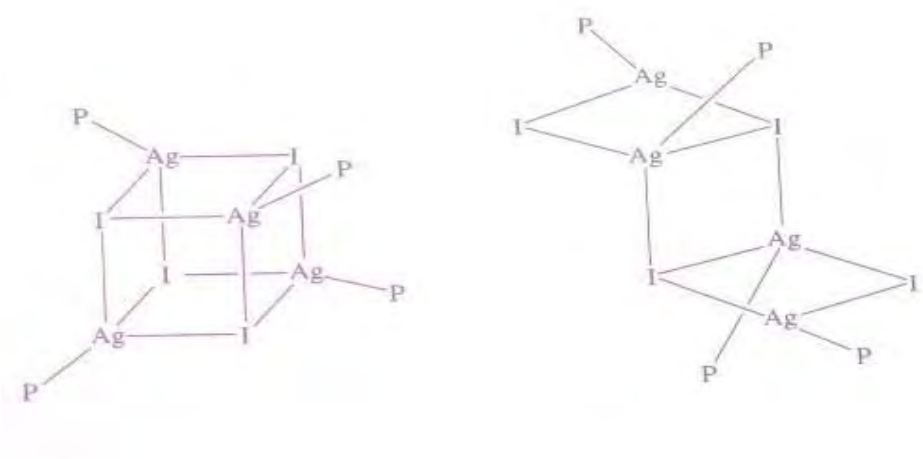



***Figure 5***: The Cube and Chain structures of $[Ag_4I_4(PPh_3)_4]$[14]

The complexes $(AgXR_3)_2$ are generally dimeric with bridging X. Triphenylphosphine forms four coordinate $[Ag(PPh_3)_4]^+$. Slightly larger phosphines, such as $PCyPh_2$ and $PCy_2Ph$ give 3-coordinate $[AgL_3]^+$, while bulky phosphines such as $PBut_3$ or $P(mes)_3$ form linear cations$[L\text{-}Ag\text{-}L]^+$.

Complexes with bridging bidentate phosphines tend to be dimers or tetramers with bridging phosphines, as in Figure 6. Phosphines with a large bite angle, (Figure 6), may however form mononuclear chelates.

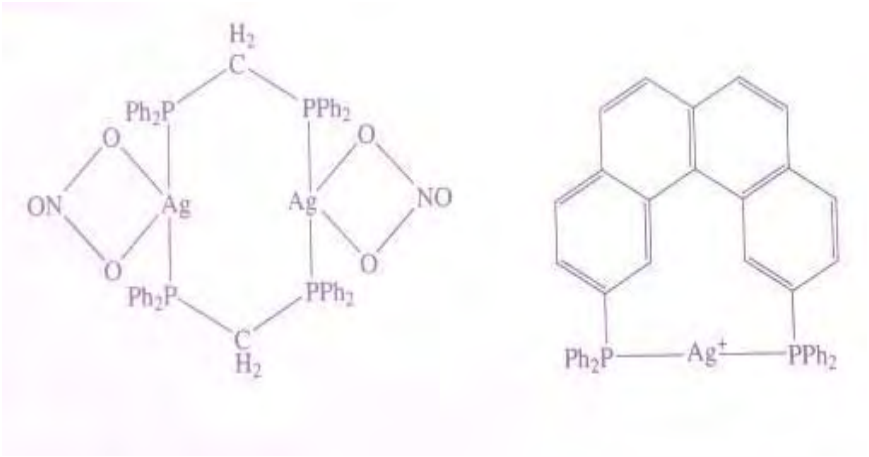



***Figure 6****:* Bridging and Chelating diphosphine derivatives of Silver[14]

### I.1.4.5 Complexes with other ligands

Silver(I) has a relatively low affinity for oxygen donors, although compounds and complexes containing carboxylate ions, DMSO, DMF, and crown ethers are known. [15] It forms numerous complexes with the donor atoms S, Se, P and As. With sulfur the thiosulphate complexes, $[Ag(S_2O_3)]^-$ and $[Ag(S_2O_3)_2]^{3-}$ are quite stable. Other important sulfur ligands for $Ag^+$ are thiolate anions, which give oligomers, $(AgSR)_n$, dithiocarbamate ions, $SCN^-$, thioureas and thioethers. Silver(I) binds to peptides and proteins, with a preference for –SR and imidazole nitrogen functionalities.

The dithiocarbamate ion $Pr_2NCS_2^-$ forms a hexanuclear complex with a trigonal antiprismatic array of silver ions. Similar anionic clusters are also formed with the related $(NC)_2C=CS_2^{2-}$ ligand, e.g. $[Ag_6L_6]^{6-}$ and $[Ag_8L_6]^{4-}$. Four-, five-, and six-coordination is found in $Ag^+$ complexes with sulphur macrocycles. For e.g.,in $[Ag(16s6)]ClO_4$ only four of the six S atoms coordinate to give tetrahedral geometry (16S6= hexathiacylohexadecane), while $[Ag(18S6)]^+$ and $[Ag(9S3)2]^+$ are octahedral. The latter complex can be oxidized to silver (II) compound. The reaction of $Ag^+$ with tetrathiometallates $MS_4^{2-}$ gives polymers $[Ag(MS_4)]_n^{n-}$(M=Mo,W).In $[NH_4]_n[Ag(WS_4)]n$ this polyanion consists of a chain of S-bridged eight membered rings (Figure 7).

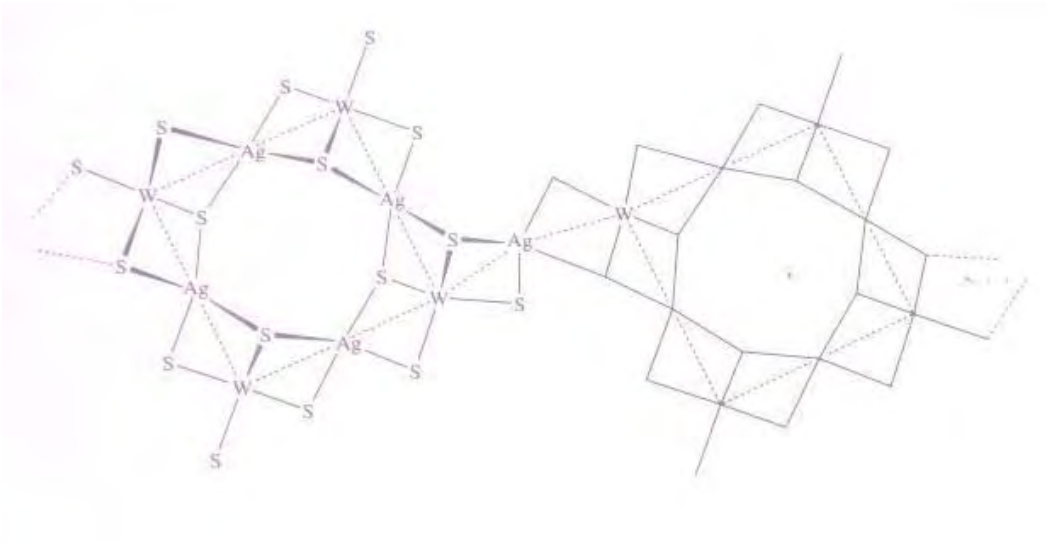


***Figure 7***: Structure of $[NH_4]_n[Ag(WS_4)]n$ [15]

## I.2 THE SILVER ION AS AN ANTIMICROBIAL AGENT

Elemental silver and silver salts have been used for decades as antimicrobial agents in curative and preventive healthcare.[16] Silver and its simple salts have found important applications in the treatment of chronic ulcers, extensive burns, and difficult-to-heal wounds. The silver ion ($Ag^+$) is the active ingredient in these simple systems and is well known as an excellent antimicrobial with high efficacy against Grampositive and Gram negative bacteria as well as a wide array of fungal microbes, but low toxicity against non target organisms.[17] Furthermore $Ag^+$ ions also exhibit virucidal properties.[18]

Silver salts and compounds that release silver ions have also found applications in materials used in medical devices such as intravascular catheters where they prevent the growth of pathogens that cause catheter-related bloodstream infections which account for a significant proportion of nosocomial infections in intensive care units.[19] More recently wound dressings containing fabrics impregnated with silver (FIS's - a new silver technology), which have antimicrobial efficacy, have been developed with the potential to provide a protective barrier against infection in severe burn wounds. Such FIS's owe their efficacy to the inclusion of discrete silver complexes which have the ability to release silver ions in a slow controlled manner.

## I.3 THE ANTIMICROBIAL MECHANISM OF ACTION OF SILVER ION

It is believed (but not yet fully understood) that the silver ions interfere with cell growth by 1. inhibition of transport functions in the cell wall (respiration), 2. interruption of cell metabolism (changing enzyme structures) and 3. inhibition of cell division (interaction with DNA) (Figure 8).[20] This multimodal efficacy, which occurs at very low concentrations, is unique to silver ion antimicrobials and reduces the possibility of developing resistant organisms.[21]

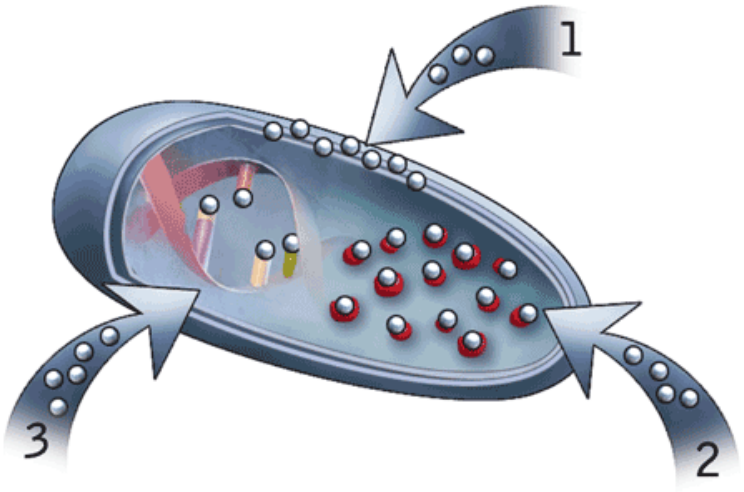



***Figure 8***: The antimicrobial mechanism of action of silver ions[20]

In 2000 Feng *et al.*[22] reported a mechanistic study of inhibition of silver ions against two different bacterial species, *S. aureus* and *E. coli*. For the experiment, both bacteria were inoculated into liquid Luria Bertoni (LB) medium and incubated at 37 °C on a rotary shaker (200 rpm) for 16 h. After that 10 µg/ml of silver nitrate was added to the liquid culture and allowed to incubate for 4–12 h. Five milliliters of the above culture was removed, centrifuged and the subsequent biomass obtained was further studied by transmission electron microscopy (TEM) and X-ray micro-analysis to find out the morphological changes occurred in the cells after treatment with silver ions. In the case of *E. coli* significant morphological changes were noticed after the treatment of silver ions. An electron-light region was observed in the center of *E. coli* cells containing some tightly condensed substance twisted together. A big gap was observed between the cytoplasm membrane and the cell wall. Presence of some electron dense granules around the cell wall was also noticed. The X-ray microanalysis of these electron dense

granules demonstrated the presence of silver and sulfur assuming that the silver ions after entering the bacterial cell might have combined with the cell components containing sulfur. Similarly, in the case of *S.aureus* the presence of condensed substance in the electron-light region was observed. The cytoplasm membrane was shrunken and detached from the cell wall. In the condensed region of *S. aureus* cells, a large amount of phosphorus was found. There were also, slight differences observed related to the effect of silver ions on *S.aureus* when compared with *E.coli*. The electron-dense granules observed in *S.aureus* and the electron-light region was darker than *E. coli* cells. *S. aureus* has a much stronger defense system compared to *E.coli*. *S.aureus* is Grampositive bacteria with a thicker peptidoglycan cell wall than *Ecoli* and there is presence of a clearly visible nuclear region in the center of cells where DNA molecules are distributed randomly. Thus, this thicker cell wall protects the cell from the penetration of silver ions in the cytoplasm.[23] By the comparative evaluation of the effects of silver ions on both the test organisms, the authors suggested the possible mechanism of action of silver ions. The silver ions enter into the bacterial cells by penetrating through the cell wall and consequently turn the DNA into condensed form which reacts with the thiol group proteins and result in cell death. The silver ions also interfere with the replication process. To the 0.05 M aqueous histidine and tryptophan solution, 0.05 M silver nitrate was added which resulted in the formation of a white precipitate. This precipitate was centrifuged, dried and used for the evaluation of antimicrobial activity by double serial dilution method. The toxicity of silver complexes of tryptophan and histidine was tested on a group of white mongrel mice. The histidine complex with silver compound showed good antimicrobial activity against Gramnegative bacteria while, the tryptophan complex with silver compound showed higher antimicrobial activity and broad spectrum of action. In the toxicity study, both the complexes of histidine and tryptophan show low toxicity. From the above experimental work it was found that the tryptophan complex with silver depicted a better antimicrobial activity than the histidine silver complex.

Bromberg *et al*[24] demonstrated the use of silver nitrate for the treatment of periodontal pathogens. They found silver nitrate more efficient than antibiotics for the treatment of oral cavity of periodontal infections.

The mechanism of action of silver is linked with its interaction with thiol group compounds found in the respiratory enzymes of bacterial cells. Silver binds to the bacterial cell wall and cell membrane and inhibits the respiration process. In the case of *E.coli*, silver acts by inhibiting the uptake of phosphate and releasing phosphate, mannitol, succinate, proline and glutamine from *E. coli* cells. Bactericidal actions of a silver ion solution on *E.coli*, is studied by energy-filtering transmission electron microscopy and proteomic analysis.

The mechanism for the antimicrobial action of silver ions is not properly understood however, the effect of silver ions on bacteria can be observed by the structural and morphological changes. It is suggested that when DNA molecules are in a relaxed state the replication of DNA can be effectively conducted. But when the DNA is in a condensed form it loses its replication ability hence, when the silver ions penetrate inside the bacterial cell the DNA molecule turns into the condensed form and loses its replication ability leading to cell death. Also, it has been reported that heavy metals react with proteins by getting attached with the thiol group and the proteins get inactivated.

Simple biocides such as $Ag^{+}$ ions generally exhibit indiscriminate microbial activity due to their multimodal nature and their ability to penetrate the outer cell layers of a range of microorganisms.

***Table 1***: Compositions of outer cell layers of different microorganisms[25]

| **Organism** | **Outer cell layers** | **Example(s)** |
|---|---|---|
| Grampositive cocci | Cell wall: predominantly Peptidoglycan | *Staphylococci* |
| Gramnegative bacteria | Outer membrane: phospholipids, Lipopolysaccharide | *P.aeruginosa, E.coli* |
| Mycobacteria | Cell wall: mycolate of a arabinogalactan | *Mycobacterium tuberculosis* |
| Bacterial spores | Outer spore coat: alkali-resistant (S-S bonds)<br>Inner spore coat: alkali-soluble (acidic polypeptides)<br>Cortex: peptidoglycan, including spore specific | *Bacillus spp* |
| Yeasts and moulds | Cell wall: chitin + chitosan<br>Cell wall: chitin + glucan<br>Cell wall: glucan + mannan | *Mucor rouxii*<br>*A.niger*<br>*S.cerevisiae, C.albicans* |
| Intestinal protozoa | Cysts have thick outer coverings | *C.parvum* |
| Other protozoa | Double-walled cysts containing cellulose (during encystation) | *A.Castellanii* |
| Algae | Cell wall: cellulose + other polysaccharides + other constituents | green (Chlorophyta), brown(Phaeop-phyta) and red (Rhodophyta) algae |

## 1.4 MICROBIAL RESISTANCE TO SILVER

Silver resistance has been reported in bacteria isolated from both clinical and environmental settings. The genetic basis of silver resistance was first reported by McHuge *et al*,[26] demonstrating that silver resistance was plasmid encoded and has been confirmed by others. The physiological, biochemical, genetic and structural studies of the silver resisitance determinant plasmid pMG 101 established the molecular basis of silver resisitance. Plasmid pMG 101 is a 182 kb, transferable plasmid encoding resistance to silver, mercury, tellurite, ampicillin, chloramphenicol, tetracylin, streptomycin and sulphonamide. The silver resistance cassette of genes encodes two silver efflux pumps and two periplasmic $Ag^+$ binding proteins.

## I.5 SILVER COMPLEXES AS ANTIMICROBIAL AGENTS

In addition to simple silver salts a number of complexes have also been used clinically.[27] Such silver complexes are particularly interesting since the antimicrobial activity and other desirable properties can be changed by varying the the number and type of ligands coordinated to the silver ion. Important factors to consider when designing novel silver based antimicrobial complexes are:

1. The type of atoms bound to the $Ag^+$ ion (O>N & S>>P)
2. The ease of ligand replacement and control of $Ag^+$ ion release.
3. Chemical and Photo-Stability (Blackening)
4. Cost

The search for new complexes and materials allowing biocidal $Ag^+$ ions to be delivered with increased efficiency is currently an active research area in inorganic medicinal and material chemistry. Silver has been described as ‘oligodynamic’ because of its ability to exert a bactericidal effect at minute concentrations[28]. In a complex biological system such as wound fluid, the maximum level of free (available) $Ag^+$ is approximately 1 µg/ml. Above this level, $Ag^+$ complexes with anions such as chloride to form minimally soluble and inactive salts resulting in costly loss of efficacy. However developing formulations which allow for the application of optimum low concentrations of simple silver salts and labile silver complexes under biological conditions can be difficult because of problems associated with the photosensitivity of the free $Ag^+$ ion. The rate of

metal ion release and the relative stability of any silver-complexes can be controlled using variations in the ligand architecture and the overall structural motif of the compound.

**Silver sulphadiazine**

Silver-sulphadiazine(AgSD)[29] (Figure 9) (which is available commercially in products such as Flammazine®) a compound that has been very successfully applied in the clinic. Upon application AgSD releases the two antibacterial agents, free $Ag^+$ ion and the sulphonamide antibiotic sulphadiazine which in the drug are combined together in a polymeric structure composed of 6 silver atoms bonding to 6 sulphadiazine molecules via labile Ag-Nitrogen linkages. The sulphadiazine also reduces the photosensitivity of the $Ag^+$ in the complex.

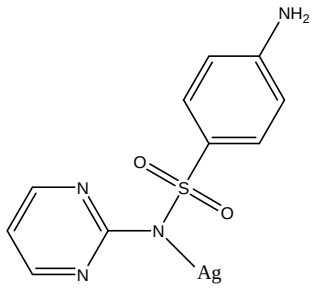



***Figure 9***: Structure of one unit of Silver-Sulfadiazine[29]

Silver sulfadiazine is used as a 1% water-soluble cream. AgSD works as a broad-spectrum antibiotic. It is used especially for the treatment of burn wounds. AgSD serves as a reservoir of silver in the wound and slowly liberates silver ions. All kinds of sulfa-drugs have been tested in combination with silver but sulphadiazine was found to be most effective. AgSD binds to cell components including DNA and cause membrane damage. It achieves bacterial inhibition by binding to the base pairs in the DNA helix and thus inhibits transcription. In a similar way it also binds to phage DNA.

In deep dermal and full-thickness burns, antiseptic agents, which can penetrate into deeper layers, such as silver-sulfadiazine should be applied. The released silver ions bind to the microbial genes (DNA) and inhibit the reproduction of bacteria and fungi. Sulfadiazine inhibits the production of folic acid which is necessary for the reproduction of bacteria. In case of later surgical debridement an unfavourable effect of silver-

sulfadiazine is that it softens the necrosis thus complicating a tangential excision. If applied broadly, the systemic resorption of silver ions may cause an impaired acid-base balance, leukopenia as well as liver and kidney damage.

A number of groups in various labs around the world are synthesizing silver complexes and testing for biological activity. A number of silver complexes have been synthesized that have been found to have chemotherapeutic potential as antimicrobial or cytotoxic agents. The antimicrobial complexes are of interest to the pharmaceutical industry for potential use as topical agents, oral antibiotics and antimicrobial coatings for medical devices. With the emergence of ubiquitous antimicrobial resistance to antibiotics and antiseptics $Ag^+$ ion technologies have re-emerged as attractive biocides for medical and industrial applications.

A number of silver complexes have also been shown to display significant cytotoxicity against selected cancer cell[30] lines and such complexes are of interest to medicinal chemists. A selection of these biologically active complexes are discussed below.

## 1.6 SILVER BASED BIOCIDAL PRODUCTS

As mentioned, silver sulfadiazine cream is used for treating burns and this is available commercially as a topical cream known as Silvadine.[31] There are also a number of antimicrobial wound dressings that contain silver such as Acticoat™ [32], SilverIon[33], Contreet[34] and Silvercel[35]. Several companies have manufactured silver antimicrobial agents intended for use in many applications. For example Agion from Agion[36], JMAC from Johnson Matthey[37] and Biomaster from Addmaster.[38]

AgIon

AgIon incorporates silver ions into a zeolite carrier and works by ion exchange. Silver ions exchange with other positive ions present in the moisture in the atmosphere.

JMAC

This is silver chloride deposited on inert titanium dioxide and it is finding applications as coatings on sutures, wound dressings, catheters and internal feeding tubes.

Biomaster

Biosilver is a product from the Biomaster range and it consisits of titanium dioxide coated with silver chloride and it is available in powder and liquid forms. It can be used for incorporation into textiles, paints and coatings.

There are also some companies which have developed silver based paints. These include Bioni Hygenic[39] and Stershield[40]. Bioni Hygenic utilizes nanosilver as the antimicrobial agent which is trapped inside a polymer matrix. This paint is currently applied in severel hospitals in Germany. Stershield use Biosilver as the antimicrobial additive in their paint and is marketed by Dulux. The use of an antimicrobial paint in hospital wards may help reduce the spread of infection. There are also a number of companies which market catheters impregnated with a form of silver.

## I.7 SILVER COMPLEXES EXHIBITING BIOLOGICAL ACTIVITY

Despite the fact that silver has a low affinity for oxygen donor ligands, such complexes are known. Silver complexes of oxygen donor ligands such as, $[Ag(hino)]_2$ (where hino = 4-isopropyltopolone) and water-soluble silver (I) complexes of (*R*)-(+)- and (*S*)-(−)-2-pyrollidone-2-carboxylic acid displayed wide ranging and effective activities against some bacteria, yeasts and moulds. It has been found that the silver–oxygen bonding properties rather than the chiral helical or achiral polymer structure play a role in exhibiting antimicrobial activities. The antimicrobial activities of Silver(I)–oxygen bonding complexes are independent of whether the ligand itself possesses antimicrobial activities. Examples of such complexes containing acetasalicyclic acid (Hasp) are; $\{[Ag(L\text{-}Hasp)]_2\}$ and $\{[Ag(L\text{-}Hasp)]_2\}_n$, where the ligand showed no activity. Similarly, salicylic acid (salH) did not prevent the growth of a fungal pathogen, while the silver complexes, $[Ag(salH)]_2$ and $[Ag(NH_3)(salH)]_2$ greatly inhibited cell reproduction. These complexes also produced a cytotoxic response against human cancer cells.

The biological action of the silver (I) oxygen complexes comes from a weaker bonding property of the Ag–O bond. In the biological system, the ease of ligand replacement of the silver (I) complexes would result in further replacement with biological ligands. The Ag–O bonding complexes can readily undergo ligand replacement with O-, N- or S-donor atoms. The antimicrobial activities of silver (I)–oxygen bonded complexes are

due to the silver (I) ion itself, i.e., due to a direct interaction between the silver (I) ion and the biological ligands such as protein, enzymes and membrane. The coordinating ligands of the silver (I) complexes play the role of carrier for the silver (I) ion to the biological system. The magnitude of antimicrobial properties of silver complexes is related to the ease with which they participate in ligand exchange reactions. For example, it has been speculated that the weak Ag–O and Ag–N bond strengths might play an important role in exhibiting a wider spectrum of antimicrobial and antifungal activities and that the potential target sites for inhibition of bacterial and yeast growth by silver complexes might be the sulfur containing residues of proteins. Generally, Ag–S complexes have been shown to have a narrower spectrum of antibacterial activity than Ag–N complexes but no antifungal activity. In contrast, the compounds with Ag–P bonds have shown no activity against bacteria, yeast or moulds.

A sulfur coordinated, water soluble silver (I) complex of thiomalic acid showed remarkable antimicrobial activity against some bacteria, yeast and moulds. Although aqueous silver nitrate itself has similar activities for bacteria, the complexation of silver (I) with thiomalate leads to appreciably high activities for some moulds. Antimicrobial activities have been observed for sulfur bonded silver complexes of 2-mercaptonicotinic acid, $[Ag(Hmna)]_6 \cdot 4H_2O$ and 2-mercaptobenzoic acid, $[Ag(Hmba)]_n$ and $[Na\{Ag(Hmba)\} \cdot H_2O]_n$. The spectra of antimicrobial activities observed in Ag–S bonded compounds have so far been narrower than those in the Ag–N bonded compounds such as $[Ag(im)]_n$ (im = imidazole) and $[Ag(triaz)]_n$ (triaz = 1,2,4-triazole). The key factor determining the spectrum of antimicrobial activity is the nature of atom coordinated to the silver (I) atom and its bonding properties, (i.e., the ease of ligand replacement), rather than the solid state structure, solubility, charge and degree of polymerization of the complexes.

In 2003 McCann *et al*[41] reported reaction of (Z)-3-(1*H*-imidazol-l-yl)-2phenylpropenenitrile (imppn) with $AgClO_4$ producing the $[Ag_2(imppn)_4(ClO_4)_2]$ (Figure 10) complex. In the dimeric Ag(I) complex each metal is coordinated to the imine nitrogens of two imppn ligands in an almost linear fashion and the two $[Ag(imppn)_2]^+$ units are linked by an Ag-Ag bond, supported by two trans bridging bidentate perchlorate groups and by π-π interactions between the ligands. *In vitro* tests on the ability of compounds to inhibit the growth of pathogenic yeast *Candida albicans*

showed that imppn and its metal complexes were markedly less effective than the prescription drug, Ketoconazole.

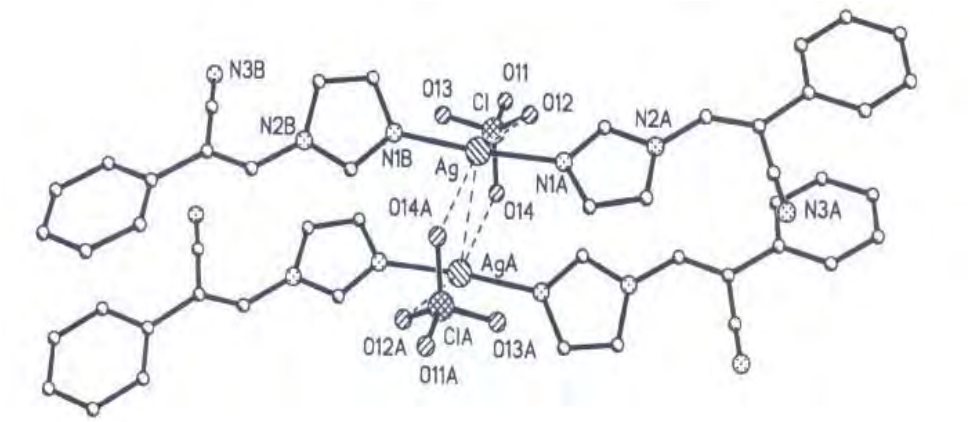



***Figure 10***: Structure of $[Ag_2(imppn)_4(ClO_4)_2]$ [41]

In 2004 Coyle *et al* [42] synthesized $[Ag_2(NH_3)_2(SalH)_2]$ from salicyclic acid and $Ag_2O$ in concentrated aqueous $NH_3$ and the dimeric Ag(I) complex was characterised using X-ray crystallography (Figure 11). The complex is centrosymmetric with each metal coordinated to a salicylate carboxylate oxygen and to an ammonia nitrogen atom in an almost linear fashion. The two $[Ag(NH_3)(salH)]$ units in the complex are linked by an Ag-Ag bond.

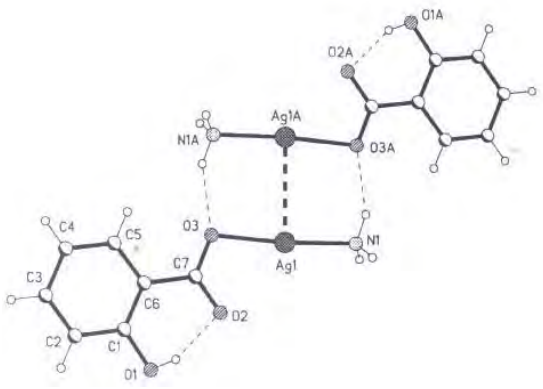



***Figure 11***: X-ray crystal structure of $[Ag_2(NH_3)_2(salH)_2]$[42]

$SalH_2$, $[Ag_2(salH)_2]$ and $[Ag_2(NH_3)_2\ (SalH)_2]$ were screened for their ability to inhibit the growth of *Candida albicans*, whilst metal-free $salH_2$ was essentially ineffective at controlling the growth of the organism, $[Ag_2(salH)_2]$ did show quite marked activity. However, the ammonia complex $[Ag_2(NH_3)_2(salH)_2]$ displayed an approximately tenfold superior activity at controlling yeast cell proliferation.

In 2004, Liu *et al* [43] reported the reaction of $Ag_2O$ and sulfamic acid in a 30% ammonia and 4% NaOH solution resulting in a http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VM7-4DTP5W1-5&_user=2322584&_coverDate=12%2F01%2F2004&_alid=771923479&_rdoc=234&_fmt=high&_orig=search&_cdi=6143&_st=5&_docanchor=&view=c&_ct=446&_acct=C000056897&_version=1&_urlVersion=0&_userid=2322584&md5=3fb49f49e3c49f0091bfa8cb963d0ed0 - hit1silverhttp://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VM7-4DTP5W1-5&_user=2322584&_coverDate=12%2F01%2F2004&_alid=771923479&_rdoc=234&_fmt=high&_orig=search&_cdi=6143&_st=5&_docanchor=&view=c&_ct=446&_acct=C000056897&_version=1&_urlVersion=0&_userid=2322584&md5=3fb49f49e3c49f0091bfa8cb963d0ed0 - hit3(I) polymer, $Na[Ag(NH_2SO_3)_2]_n$ (Figure 12). The X-ray crystal structure analysis indicates that the complex is a http://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VM7-4DTP5W1-5&_user=2322584&_coverDate=12%2F01%2F2004&_alid=771923479&_rdoc=234&_fmt=high&_orig=search&_cdi=6143&_st=5&_docanchor=&view=c&_ct=446&_acct=C000056897&_version=1&_urlVersion=0&_userid=2322584&md5=3fb49f49e3c49f0091bfa8cb963d0ed0 - hit2silverhttp://www.sciencedirect.com/science?_ob=ArticleURL&_udi=B6VM7-4DTP5W1-5&_user=2322584&_coverDate=12%2F01%2F2004&_alid=771923479&_rdoc=234&_fmt=high&_orig=search&_cdi=6143&_st=5&_docanchor=&view=c&_ct=446&_acct=C000056897&_version=1&_urlVersion=0&_userid=2322584&md5=3fb49f49e3c49f0091bfa8cb963d0ed0 - hit4 polymer through Na–O bonds forming a 3D framework. And the complex shows high cytotoxicity properties to normal cells and carcinoma cells.

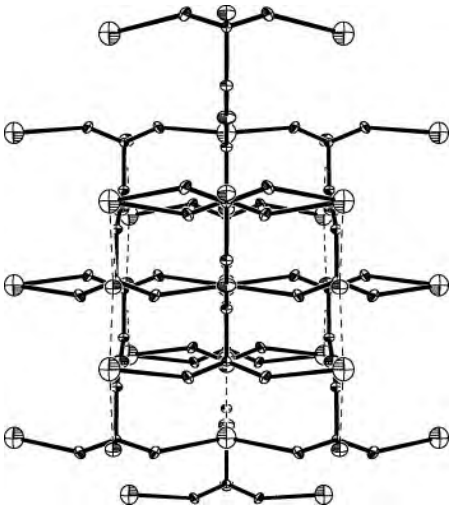


***Figure 12***: The structure of $Na[Ag(NH_2SO_3)_2]_n$[43]

In 2004 five Ag(I) complexes containing the ligands bis(imidazol-2-yl)methane (2-BIM) and its derivatives were reported by Abuskhuna *et al*[44] and $[Ag_2(2BIM)_2]ClO_4)_2$ and $[Ag_2(2\text{-}BIM(Bz)OH)_2](ClO_4)_2.EtOH$ were characterized using X-ray crystallography. In each dimer the two Ag(I) ions are two-co-ordinate and there are small but definite argentophilic Ag-Ag($d^{10}$-$d^{10}$) interactions. All of the complexes display antifungal activity when tested in vitro against the fungal pathogen *Candida albicans*.

The X-ray crystal structure of $[Ag_2(2\text{-}BIM)_2](ClO_4)_2$ (Figure 13) showed the complex to be centrosymmetric, containing two $Ag(2\text{-}BIM)^+$ units. The two metal ions are two-coordinate and have identical atoms in the plane of the chelating ligand. Using its two imine N atoms each 2-BIM ligand bridges the pair of Ag(I) ions. All four N atoms (N1, N4A, N4, N1A) are coplanar and the two imidazole groups in each 2-BIM ligand have an interplanar angle of 75.52(8)°.

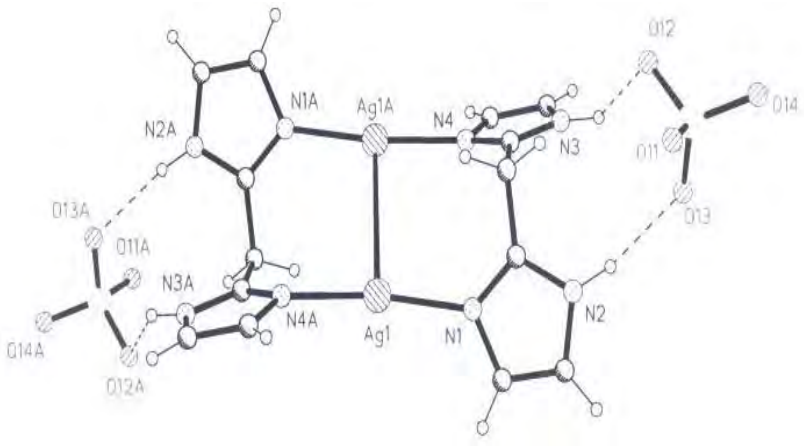



***Figure 13***: X-ray crystal structure of $[Ag_2(2\text{-}BIM)_2](ClO_4)_2$[44]

The X-ray crystal structure of $[Ag_2(2\text{-}BIM(Bz)\text{-}OH)_2](ClO_4)_2.EtOH$ (Figure 14) shows the asymmetric unit containing one $[Ag_2(2\text{-}BIM(Bz)\text{-}OH)_2]^{2+}$ unit, two perchlorate anions and a solvate ethanol. The two Ag(I) ions are again bridged by the two ligands and each metal is approximately linearly coordinated to a pair of imine nitrogens. There are additional longer interactions with the perchlorate anions. The metal-metal distance of 3.018(4)Å is considerably shorter than for the $[Ag_2(2\text{-}BIM)_2](ClO_4)_2.EtOH$ complex and there appears to be some degree of intermolecular π-π interaction between the imidazole and phenyl rings of the opposing two 2-BIM(Bz)OH ligands in the dimer.

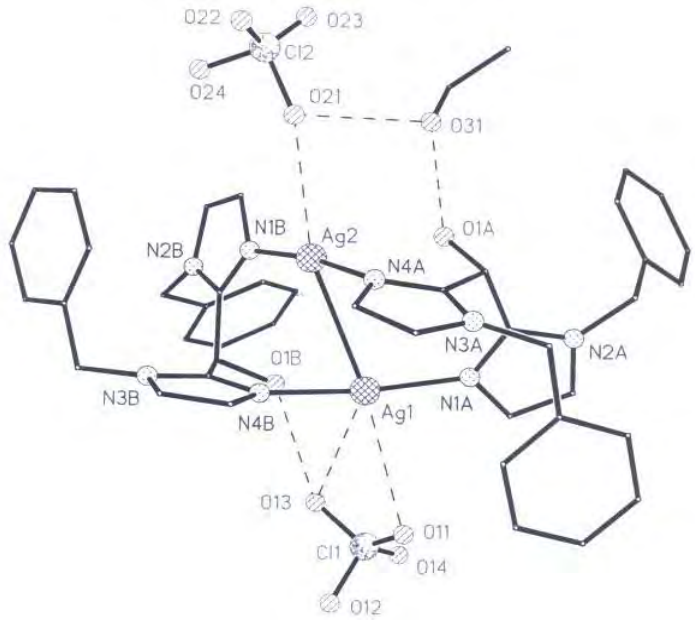



***Figure 14***: X-ray crystal structure of $[Ag_2(2\text{-}BIM(Bz)\text{-}OH)_2](ClO_4)_2.EtOH$.[44]

All of the metal-free ligands were found to be inactive against the fungal cells. As aqueous suspensions, the silver complexes were moderately active with MIC value ranges indicated in brackets:$[Ag_2(2\text{-}BIM)_2](ClO_4)_2$ (10-20µg/$cm^3$); $[Ag_2(2\text{-}BIM(Bz)OH)_2](ClO_4)_2$.EtOH (50-100µg/$cm^3$); $[Ag_2\{2\text{-}BIM(Me)\}_2](ClO_4)_2$ (20-50 µg/$cm^3$) $[Ag_2\{2\text{-}BIM(CN)\}_2](ClO_4)_2$ (20-50 µg/$cm^3$).

A considerable improvement in antifungal activity was observed upon testing the complexes as DMSO/water solutions as opposed to aqueous suspensions: $[Ag_2(2\text{-}BIM)_2](ClO_4)_2$ (5-10µg/$cm^3$); $[Ag_2(2\text{-}BIM(Bz)OH)_2](ClO_4)_2$.EtOH (2.5-5µg/$cm^3$); $[Ag_2\{2\text{-}BIM(Me)\}_2](ClO_4)_2$ (2.5-5µg/$cm^3$); $[Ag_2\{2\text{-}BIM(CN)\}_2](ClO_4)_2$ (5-10 µg/$cm^3$).

The highly fluorinated tris(pyrazolyl)borate ligand $[HB(3,5\text{-}(CF_3)_2Pz)_3]^-$ has been used in the isolation of the air- and light stable silver complex, $[HB(3,5\text{-}(CF_3)_2Pz)_3]Ag(OSMe_2)$ as reported by Rasika Dias *et al*[45] in 2006. It is a monomeric tetrahedral silver complex with O-bonded dimethylsulfoxode ligand (Figure 15). The silver adduct $[HB(3,5\text{-}(Cf_3)_2Pz)_3]Ag(OSMe_2)$ and the related $[HB(3,5\text{-}(CF_3)_2Pz)_3]Ag(THF)$ (where $OSMe_2$= dimethyl sulfoxide; THF= tetrahydrofuran) show good antibacterial activity, and their antibacterial efficacy against staphylococcus aureus is greater than those of $AgNO_3$ and silver sulphadiazine.

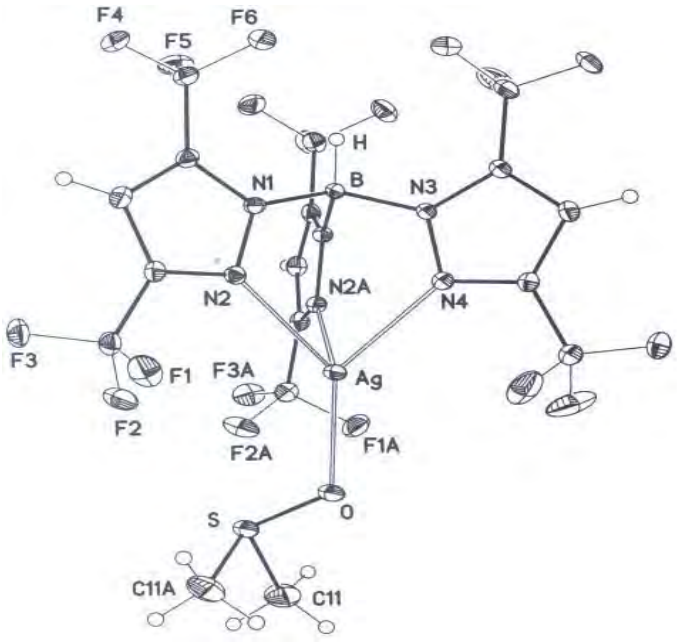



***Figure 15***: X-ray crystal structure of $[HB(3,5\text{-}(Cf_3)_2Pz)_3]Ag(OSMe_2)$[45]

In 2007, Lei Zhang *et al*[46] reported two new polymeric silver (I)-fluconazole complexes: $[Ag(HFlu)(NO_3)]_n$ and $\{[Ag(HFlu)_2](ClO_4)\}_n$ (Figures 16 and 17). The crystal structure of $[Ag(HFlu)(NO_3)]_n$ consists of infinite 1D single strand helical coordination arrays with alternative...pmpm... arrangements, which are interlinked through hydrogen bonding interactions to generate a 3D network. The shortest intrachain Ag…Ag distance bridged by HFlu ligand is 8.287(1) Å. In $\{[Ag(HFlu)_2](ClO_4)\}_n$, each Ag(I) ion is coordinated by four triazole N atoms from four HFlu ligands to form a 2D coordination layer, which has a helical arrangement along the direction. The results of anti-fungal studies demonstrate that both silver (I) complexes are more active in comparison to the fluconazole drug.

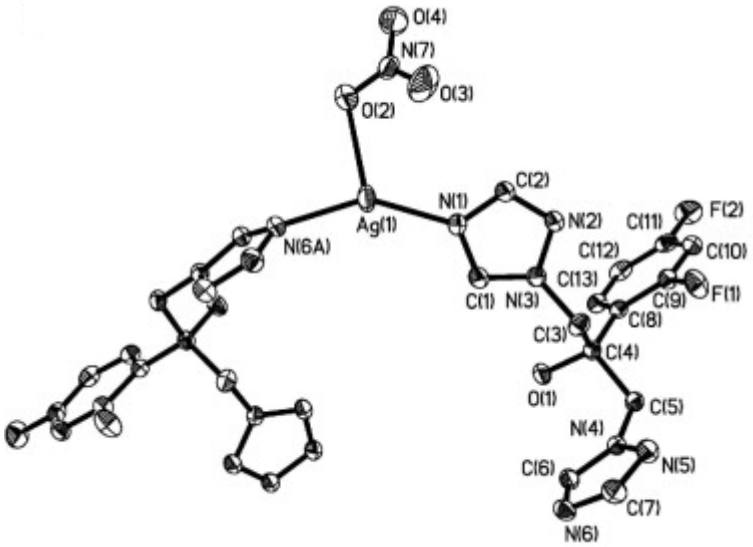



***Figure 16***: The structure of $[Ag(HFlu)(NO_3)]_n$[46]

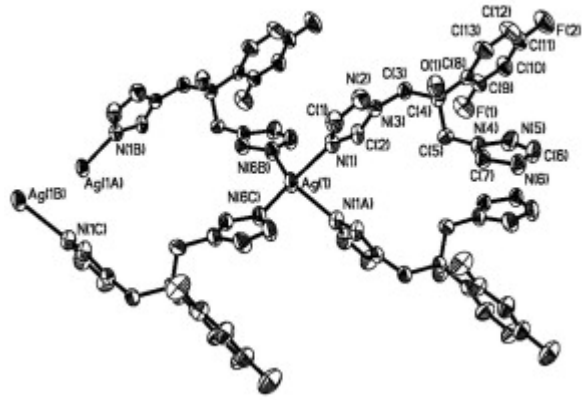



***Figure 17***: The structure of $\{[Ag(HFlu)_2](ClO_4)\}_n$[46]

$Ag_4(9\text{-aca})_4(NH_3)_2]$ [47] was shown to be over 30 times more active against *C. albicans* than the commonly used antifungal agent ketoconazole (Table 2). Although $[Ag_2(9\text{-aca})_2]_n$ appears to be only half as active as $[Ag_4(9\text{-aca})_4(NH_3)_2]$, when their $MIC_{100}$ values are equated to their silver ion content (58 μM and 56 μM, respectively) then both complexes display approximately equal activity. Against MRSA and *E. coli* $[Ag_2(9\text{-aca})_2]_n$ and $[Ag_4(9\text{-aca})_4(NH_3)_2]$ both appeared to perform significantly better than the topical antibacterial agent silver(I) sulfadiazine. These two complexes also exhibited significant cytotoxic activity against liver and lung cancer derived cells (HepG and A.498 repectively).

***Table 2:*** Antimicrobial activity (μM concentrations)[47]

| **Drug** | ***C.albicans*** **$MIC_{100}$** | **MRSA** **$MIC_{50}$** | ***E.coli*** **$MIC_{50}$** | **Hep-$G_2$** **$IC_{50}$** | **A-498** **$IC_{50}$** |
|---|---|---|---|---|---|
| $[Ag_2(9\text{-aca})_2]_n$ | 0.29 | 55.91 | 61.53 | 27.8 | 30.0 |
| $[Ag_4(9\text{-aca})_4(NH_3)_2]$ | 0.14 | 28.36 | 40.73 | 3.6 | 5.5 |
| Ketoconazole | 4.70 | | | | |
| Silver(I) sulfadiazine | | 120.40 | 154.00 | | |
| Cisplatin | | | | 15.0 | 14.0 |

Organo silver complex exhibiting biological activityare rare in the literature. The simple alkyl complexes AgR are thermally unstable.[48] The stability decreases with increasing chain length of R, thermolysis gives a mixture of alkenes and alkanes. Vinyl and aryl silver compounds are more readily accessible, usually by the reaction of a mild agent ($ZnR_2$, $PbR_4$) with silver nitrate:

$$AgNO_3 + ZnAr_2 \longrightarrow AgAr + ArZn(NO)_3$$

They are sensitive to light, air and moisture. Alkyl compounds stabilized by donor ligands are significantly more stable, for example Figure 18. The linear L-Ag-C arrangement is typical.

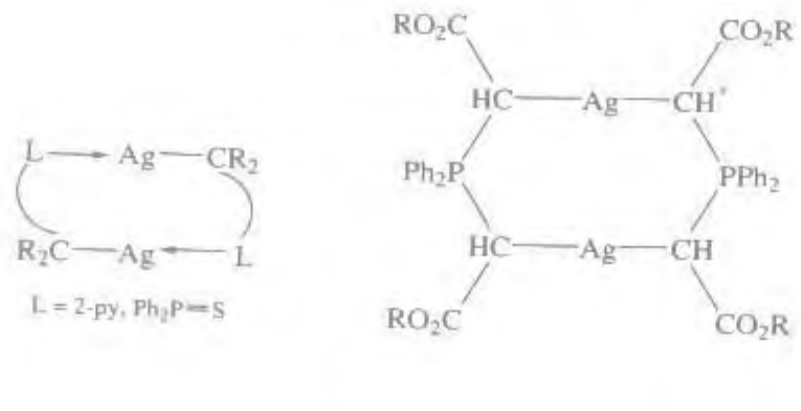



***Figure 18***: Alkyl compounds stabilized by donor ligands [48]

Silver perfluoroalkyl compounds are thermally much more stable. For example, $(CF_3)_2CFAg(NCMe)$ decomposes above 60ºC. The adducts $CF_3AgPR_3$ are photosensitive but are oxidized by air to stable $Ag^{3+}$ anion $[Ag(CF_3)_4]^-$. Complexes with the strongly electron- withdrawing pentaflouro- and pentachlorophenyl ligands are stable to water and oxygen, e.g., the yeild adduct $(C_6F_5)Ag(CH_2PPh_3)$.

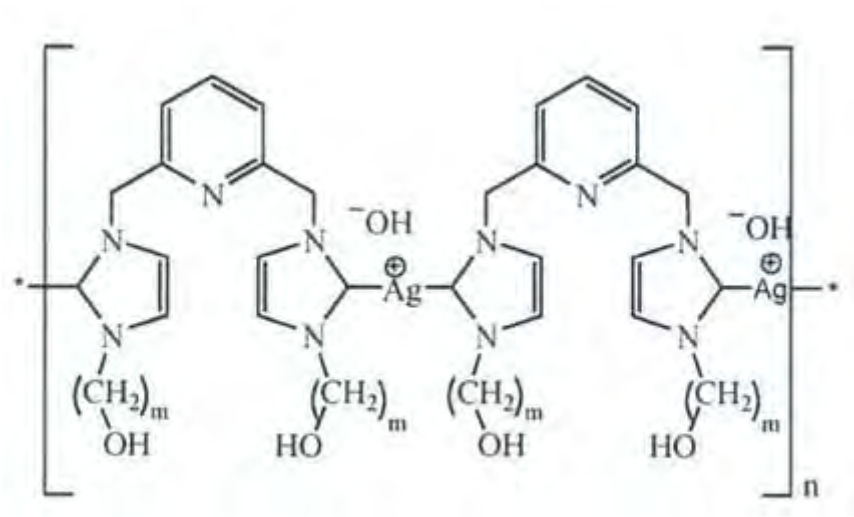
Alkynyl silver compounds are readily accessible from $AgNO_3$ and HC=CR in methanol or water in the presence of base and they are thermally stable. Like many heavy metal acetylides, silver compounds of unsubstituted acetylene are shock sensitive and explosive.

With an excess of alkylating agents linear argentite(I) anions are formed, $[R\text{-}Ag\text{-}R]^-$. These may associate to clusters, such that as in $[Li_2Ag_3Ph_6]^-$, where three $[Ph\text{-}Ag\text{-}Ph]^-$ units are held together by Ph...Li interactions.

Complexes with alkenes and arenes are formed when the hydrocarbons are shaken with aqueous solutions of silver(I) salts. Di- or polyalkenes often give crystalline compounds with $Ag^+$ bound to one to three double bonds. The formation of alkene complexes of varying stability may be used for the purification of alkenes, or for the separation of isomeric mixtures (e.g., 1,3-, 1,4-, and 1,5- cyclooctadienes), or of the optical isomers of α- and β-pinene. There is very little back-bonding contribution in the formation of $Ag^I$ π-complexes. For example, the planar complex $(hfa)Ag(Ph\text{-}C{=}C\text{-}Ph)$[47] (hfa= hexafluoroacetylacetonate) contains an almost linear acetylene ligand with a C=C bond that is only marginally longer than in free diphenylacetylene, while the Ag-C bonds are long (2.26Å).

Until recently, isolable CO complexes of silver were unknown. However, if the counteranion possesses only very weak basicity, fairly stable CO adducts are obtained. Carbon monoxide acts in these compounds as a σ-donor ligand only. Back-bonding is virtually absent and the C-O stretching frequencies are substantially higher than that of free CO (2143 $cm^{-1}$). The compounds $[Ag(CO)]^+X^-$ ($\nu_{co}$= 2204 $cm^{-1}$) and $[OC\text{-}Ag\text{-}CO]^+X^-$ ($\nu_{co}$= 2198 $cm^{-1}$) [X=$B(OTeF_5)_4$] were characterized by X-ray diffraction. The $[Ag(CO)_3]^+$ ion is formed under CO pressure.

As shown in Table 3, the carbene–silver complexes, **2a** and **2b**, shown in Figure 19 showed better bacteriostatic effect (lower MIC value) than silver nitrate at about 2.7 times lower initial silver ion concentration.[49] This result showed that although the theoretical amounts of the silver cations released from carbene–silver complexes were lower than silver nitrate, more silver cations were in the solution from carbene–silver complexes. Most of the silver cations from silver nitrate were precipitated as silver chloride and lost activity. The amount of 0.1% chloride anions in the culture medium is close to physiological concentrations of chloride (0.15 M sodium chloride). Under these conditions, carbene–silver complexes were more stable than silver nitrate. Moreover, when the solutions demonstrating the lowest MIC value were inoculated onto agar plates, the growth of organisms treated with carbene–silver complexes was delayed for a longer time than was the growth of organisms treated with silver nitrate. The observed results can be explained by the slow decomposition of the silver–NHC complexes in the aqueous culture medium to imidazolim cation and biologically active silver species. Carbene–silver complexes were observed to decompose over a period of weeks in deionized water.




**2a, 2b**

***Figure 19***: Structure of complex 2a and 2b[49]

***Table 3***: MIC results of the silver compounds[49]

| Test compounds | Ag (mg/mL) | *E. coli* | | *P. aeruginosa* | | *S. aureus* | |
|---|---|---|---|---|---|---|---|
| | | Day 1 | Day 2 | Day 1 | Day 2 | Day 1 | Day 2 |
| **2a** | 1186 | − | − | − | − | − | − |
| 1DF | | − | + | − | − | − | + |
| 2DF | | − | + | − | + | + | |
| 3DF | | + | | + | | + | |
| 4DF | | + | | + | | + | |
| **2b** | 1125 | − | − | − | − | − | − |
| 1DF | | − | + | − | + | − | + |
| 2DF | | − | + | − | + | − | |
| 3DF | | + | | + | | + | |
| 4DF | | + | | + | | + | |
| $AgNO_3$ | 3176 | − | + | − | + | + | |
| 1DF | | + | | + | | + | |
| 2DF | | + | | + | | + | |
| 3DF | | + | | + | | + | |
| 4DF | | + | | + | | + | |

DF: dilution factor (1 mL); growth (+); no growth (−).

## I.8 SILVER COMPLEXES CONTAINING PHOSPHINE

### I.8.1 Silver Phosphine Complexes exhibiting Biological Activity

Three novel silver(I) complexes consisting of both hard Lewis bases (O and N atoms) and one soft Lewis base (P atom) ((DL-a-alaninato)(triphenylphosphine)silver(I) (**1**), (DL-asparaginato)(triphenylphosphine)silver(I) **(2**) and (Lasparaginato)(triphenylphosphine)silver(I) (**3**)) were prepared from stoichiometric reactions of amino acid–silver(I) complexes with PPh3 in a 1:1 molar ratio in a mixed organic solvent.

The antimicrobial activities of the silver (I) complexes $\{[Ag(dl\text{-}ala)(PPh_3)]_2 \cdot 2H_2O\}$, $\{[Ag(dl\text{-}asn)(PPh_3)]_2 \cdot 2EtOH \cdot 2H_2O\}$,$\{[Ag(l\text{-}asn)(PPh_3)]_2 \cdot 2EtOH \cdot H_2O\}$are listed in Table 4.[50] Water-insoluble $Ag_2O$ showed modest activity against two bacteria, whereas the aqueous $Ag^+$ ion in $AgNO_3$ solution, showed effective activity against Gramnegative bacteria (*Escherichia coli* and *Pseudomonas aeruginosa*), modest activity against Grampositive bacteria (*Bacillus subtilis*), and no activity against yeasts and moulds. Complex $\{[Ag(dl\text{-}ala)(PPh_3)]_2 \cdot 2H_2O\}$showed moderate antimicrobial activities against the selected bacterium (*Staphylococcus aureus*), and modest antimicrobial activities against bacteria (*E. coli, B. subtilis* and *P. aeruginosa*) and yeasts (*Candida albicans* and *Saccharomyces cerevisiae*); however, its effectiveness was less than that of (DL-alaninato) silver(I). Complexes $\{[Ag(DL\text{-}asn)(PPh_3)]_2 \cdot 2EtOH \cdot 2H_2O\}$, and $\{[Ag(l\text{-}asn)(PPh_3)]_2 \cdot 2EtOH \cdot H_2O\}$showed favourable antimicrobial activities against four selected bacteria and moderate to modest activities against two selected yeasts. The MIC values of complexes **2** and **3** are comparable to those of the precursors, except for moulds. These results support the conclusion that the number of coordinating $PPh_3$ ligands per silver(I) atom in the complexes significantly influences the antimicrobial activities and presumably the ligand-exchangeability of the silver (I) complexes.

***Table 4***: Antimicrobial activities of silver(I) complexes **1**–**3** evaluated by using minimum inhibitory concentration (MIC; μg/ml)[50]

| Organism | {[Ag(DL-ala)(PPh3)]$_2$. 2H$_2$O} (**1**) | {[Ag(DL-asn)(PPh3)]$_2$ 2EtOH. 2H$_2$O} (**2**) | {[Ag(L-asn)(PPh3)]2 2EtOH. H2O} (**3**) |
|---|---|---|---|
| *Escherichia coli* | 125 | 62.5 | 31.3 |
| *Bacillus subtilis* | 125 | 31.3 | 15.7 |
| *Staphylococcus aureus* | 62.5 | 62.5 | 62.5 |
| *Pseudomonas aeruginosa* | 500 | 125 | 62.5 |
| *Candida albicans* | 500 | 250 | 62.5 |
| *Saccharomyces cerevisiae* | 500 | 125 | 31.3 |
| *Aspergillus niger* | >1000 | >1000 | 125 |
| *Penicillium citrinum* | 1000 | >1000 | 125 |

Antibacterial and antifungal activities of [Ag(tetz)]$_n$, [Ag(tetz)(PPh$_3$)$_2$]$_n$, [Au(tetz)(PPh$_3$)] and the free ligand Htetz (where Htetz= tetrazole), were evaluated by MIC.[51]

Antimicrobial activity of the complex [Ag(tetz)(PPh$_3$)$_2$]$_n$ was estimated as >1000 μg ml$^{-1}$ for bacteria, yeast and mould, showing no activity. The free Htetz ligand and complex [Au(tetz)(PPh$_3$)] showed only poor activities against Grampositive bacteria (*B. subtilis*, *S. aureus*). On the other hand, the precursor [Ag(tetz)]$_n$ has shown effective activities against Grampositive and negative bacteria, and yeast, but no activities against mould. These facts are consistent with the recently observed results; the polymeric silver (I) complexes without a PPh$_3$ ligand such as [Ag(im)]$_n$] (im=imidazole), [Ag(1,-triz)]$_n$(triz= triazole) and [Ag(1,2,4-triz)]$_n$ have shown effective antimicrobial activities, while almost all of their triphenylphosphine derivatives such as [Ag(im)(PPh$_3$)$_3$], have shown no activity (>1000 μgml$^{-1}$). These facts have been attributed to the restricted ligand exchange ability of the Ag---P bonding complexes. From a viewpoint of metal-based drug design, no activity of the PPh$_3$ derivatives is also crucial.

In 2003, Tao WuF *et al*[52] synthesized a novel trinuclear silver (I)- triphenylphosphine complex with nitrogen-containing hetrocyclic ligand benzimidazole (Hbim). [Ag$_3$(μ-

bim)$_3$(PPh$_3$)$_5$], was synthesized by the reaction of the precursor complex [Ag(bim)]$_n$ with two equivalents of PPh$_3$ in dichloromethane. The complex has been identified by IR, UV/VIS, EA, and X-ray diffraction crystallography. Three silver ions are bridged by three bim- ligands to form an asymmetric twelve–membered ring structure with rare twisted conformation (Figure 20). Each silver (I) ion occupied a three- or four co-ordination environment bound to one or two triphenylphosphine(s).

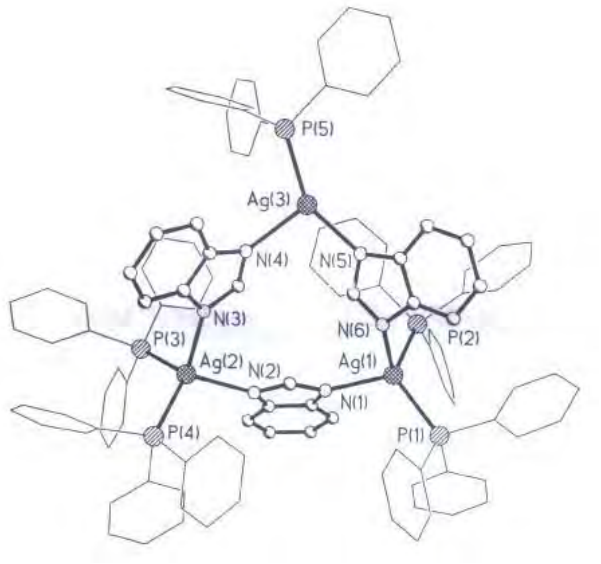



***Figure 20***: Molecular structure of [Ag$_3$(μ-bim)$_3$(PPh$_3$)$_5$] [51]

In 2005 Li *et al*[53] reported four new luminescent silver(I) sulfonate complexes with PPh$_3$, namely Ag(L1)(PPh$_3$)$_2$, Ag(L2)(PPh$_3$)$_3$, g$_2$(L3)(PPh$_3$)$_4$(H$_2$O)].1.5CH$_3$CN.0.5H$_2$O and [Ag$_4$(L4)(PPh$_3$)$_{10}$].8H$_2$O, where L1= p-toluenesulfonate, L2= 1-naphthalenesulfonate, L3= 3-carboxylate- 4- hydroxybenzenesulfonate,L4= 1, 3,6, 8-pyrenetetrasulfonate (structure of L1-L4 shown in Figure 21) and PPh$_3$= triphenylphosphine. The crystal structures were determined by single crystal X-ray diffraction method. The complexes adopt discrete structures (Figure 22-25) rather than polymeric structures. Compounds Ag(L1)(PPh$_3$)$_2$, and Ag(L2)(PPh$_3$)$_3$ show mononuclear structure while Ag$_2$(L3)(PPh$_3$)$_4$(H$_2$O)].1.5CH$_3$CN.0.5H$_2$O and [Ag$_4$(L4)(PPh$_3$)$_{10}$].8H$_2$O are dinuclear and tetranuclear molecules, respectively. Moreover the numbers of PPh$_3$ molecules coordinating to one silver center are two or three.

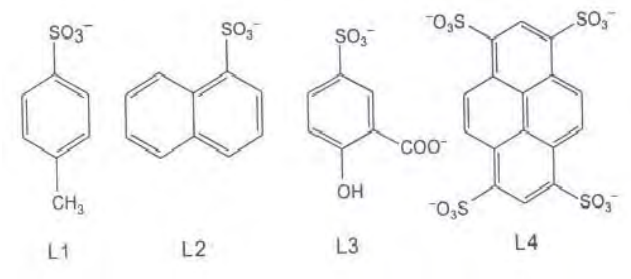



***Figure 21***: The structures of the sulfonate ligands[53]

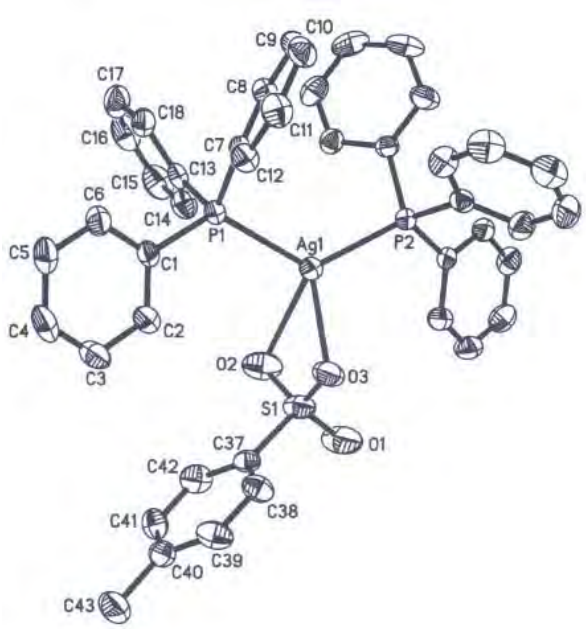



***Figure 22:*** Molecular structure of $[Ag(L1)(PPh_3)_2]$ [53]

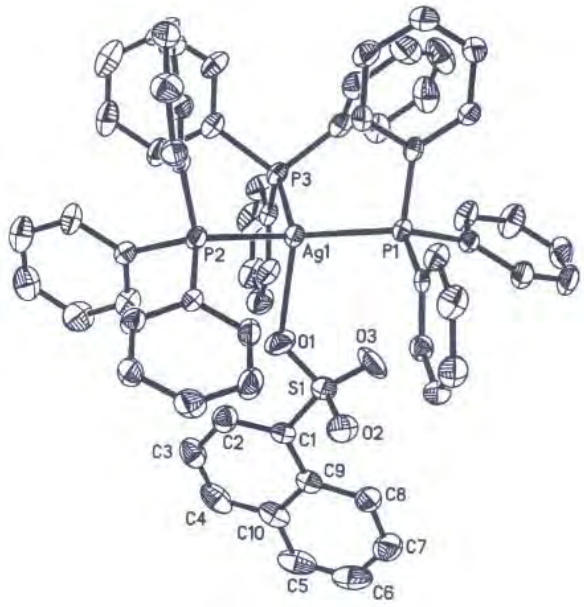



***Figure 23***: Molecular structure of $[Ag(L2)(PPh_3)_3]$[53]

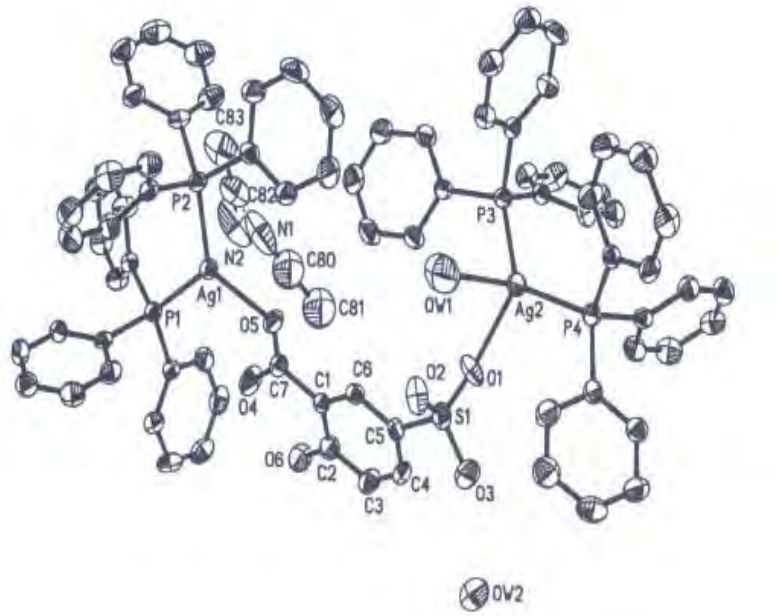



***Figure 24***: Molecular structure of $[Ag_2L3(PPh_3)_4(H_2O)].1.5CH_3CN.0.5H_2O$[53]

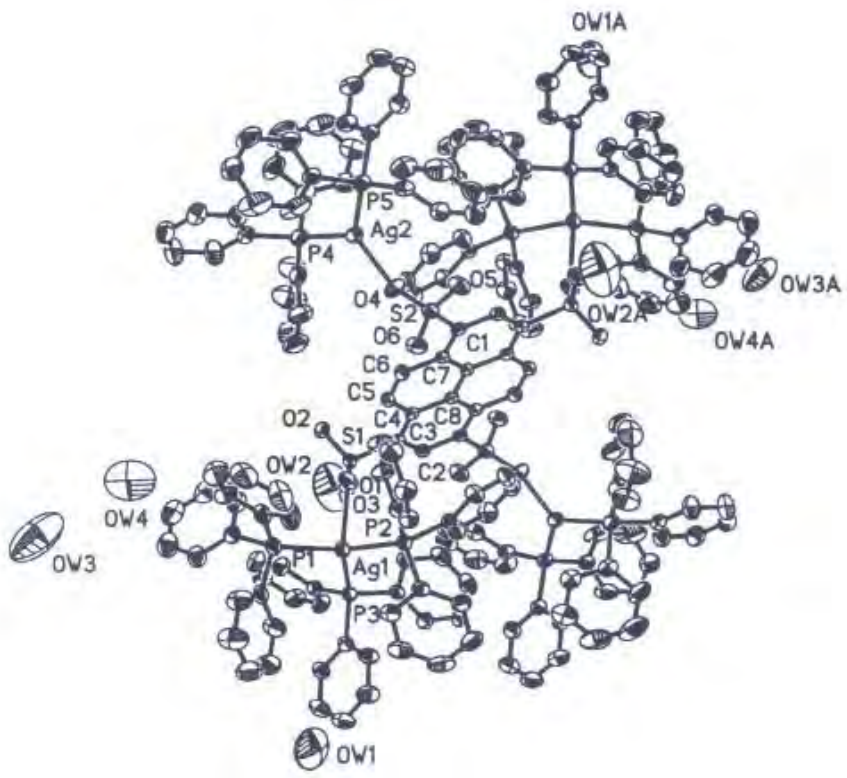



***Figure 25***: Molecular structure of $[AgL4(PPh_3)_{10}].8.H_2O$[53]

In 2005 Noguchi *et al*[54] reported a novel tetranuclear silver(I) cluster, $[Ag_2(Himdc)(PPh_3)_2]_2$ ($H_3imdc$ = imidazole-4-5-dicarboxylic acid) which was obtained by a reaction of the Ag-O bonding precussor $[Ag(R\text{-}Hpyrrld)]_2$ ($H_2pyrrld$= 2-pyrrolidone-5-carboxylic acid), $PPh_3$ and $H_3imdc$. The mononuclear complex, $[Ag(H_2imdc)PPh_3)_2]$ , was also formed by the reactions using increased amounts of $PPh_3$ . In the solid state, the complex $[Ag_2(Himdc)(PPh_3)_2]_2$ was "bivalve"- like the $Ag_4$ cluster (Figure 26), while complex $[Ag(H_2imdc)PPh_3)_2]$ (Figure 27) showed a supramolecular arrangement of 4-coordinate $AgP_2(N_2O)$ unit via an intermolecular hydrogen bonding interaction.

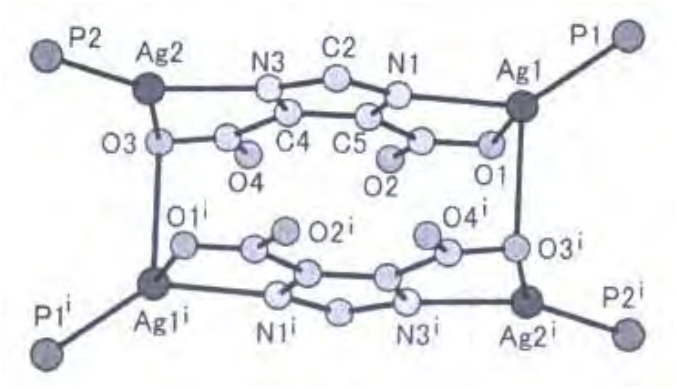



***Figure 26***: Molecular structure of $[Ag_2(Himdc)(PPh_3)_2]_2$[54]

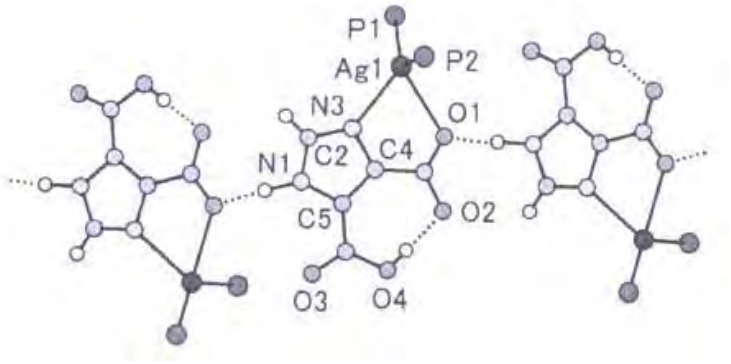



***Figure 27***: Crystal and molecular structure of $[Ag(H_2imdc)PPh_3)_2]_2$[54]

In 2008 Ardizzoia *et al*[55] reported the crystal structure of a compound composed of dimers of $[Ag(H_2L^1)(PPh_3)]_2$ formula lying on a crystallographic twofold axis, the asymmetric unit being composed by one silver (I) ion, one $H_2L^1$ and one $PPh_3$ ligand (Figure 28). Each metal centre possesses a slightly distorted trigonal stereochemistry and is coordinated to two triazole nitrogen atoms of two distinct $H_2L^1$ moieties and to the phosphorous atom of one phosphine ligand. The two $H_2L^1$ ligands, acting in the *N*,*N*′-exobidentate mode, bridge metal centres 3.72 Å apart, and form dimers in which the six-membered rings composed by the four coordinated nitrogen atoms and the two silver (I) centres adopt a boat-shape disposition. The oxygen atoms of the –OH groups are not involved in the coordination to the metal centres, as expected for a metal with soft nature like Ag(I). Nevertheless, intermolecular hydrogen bonds of moderate strength (H–D…A 2.63 Å) are present between the hydroxy groups and the neighbouring iminic nitrogen atoms.

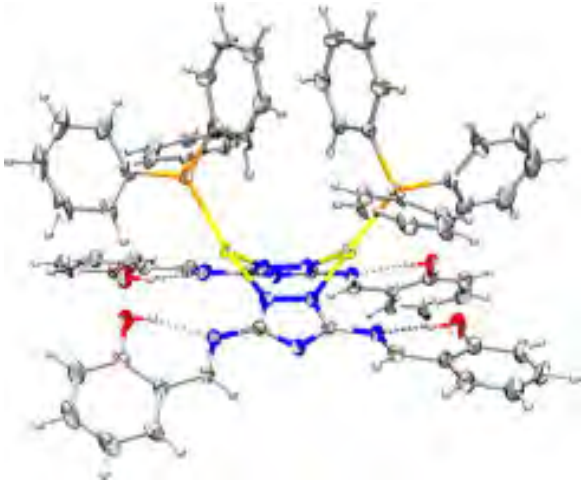


***Figure 28***: The structure of $[Ag(H_2L^2)(PPh_3)]_2$ [55]

In 2008, Zhang *et al*[56] reported the X-ray single crystal structure of $[(Ph_3PAgO_3SCH_3)_4 \cdot 4CH_2Cl_2]$ (Figure 29) and $[(Ph_3P)_2AgO_3SCH_3 \cdot CH_2Cl_2]$. Because of the different molar ratio of triphenylphosphine with silver methylsulofonate, the complex $[(Ph_3P)_2AgO_3SCH_3 \cdot CH_2Cl_2]$ is a monomer (Figure 30) with each silver atom coordinated by two $PPh_3$ groups. Complex $[(Ph_3PAgO_3SCH_3)_4 \cdot 4CH_2Cl_2]$, however, is a tetramer with the silver atom coordinated by one $PPh_3$ group.

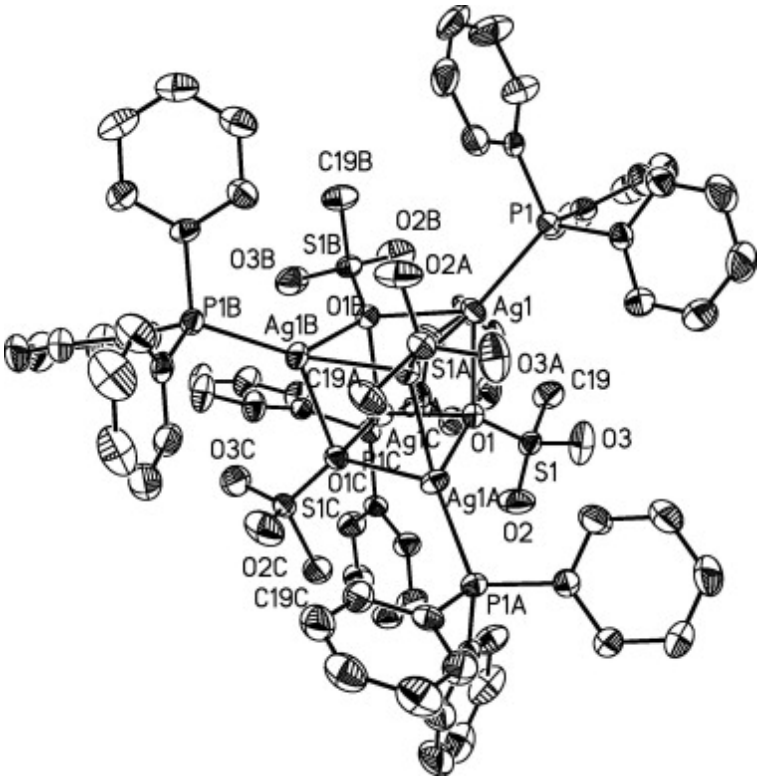



***Figure 29***: Crystal structure of $[(Ph_3PAgO_3SCH_3)_4 \cdot 4CH_2Cl_2]$ [56]

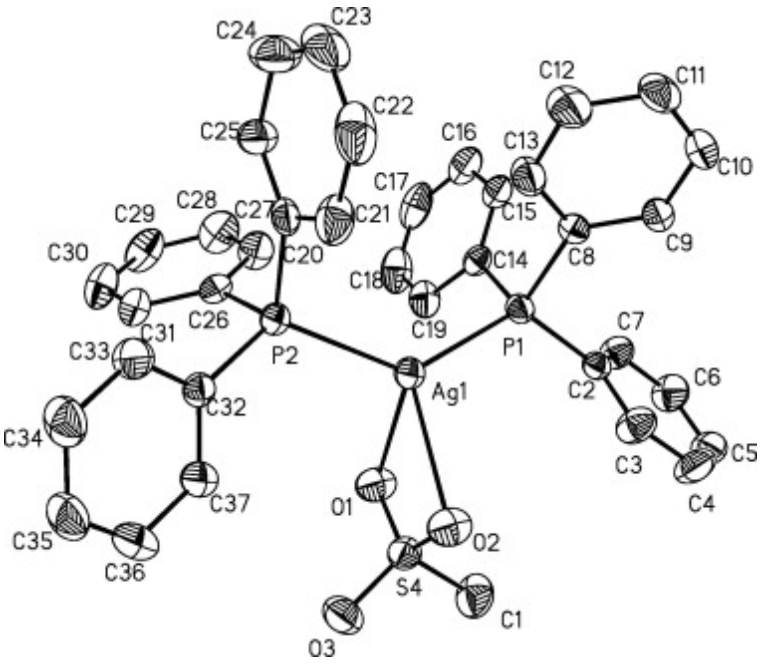



***Figure 30***: Crystal structure of $[(Ph_3P)_2AgO_3SCH_3 \cdot CH_2Cl_2]$[56]

## I.9 METAL CARBOXYLATE CHEMISTRY

### I.9.1 Coordination modes of monocarboxylic acids

Carboxylates serve as an important class of ligand in inorganic and bioinorganic chemistry.[57] The versatility of the $RCO_2^-$ ligand is attributed to the wide range of coordination modes that it can adopt. The coordination chemistry of monocarboxylic acids is well established, and a large number of carboxylate complexes have been structurally characterized. In metal carboxylates the positively charged metal centres ($M^{n+}$) are found in combination with negatively charged carboxylate groups ($RCO_2^-$), and the bonding between the metals and the carboxylate group ranges from ionic to polar covalent. For a given type of compound (i.e. a given metal, oxidation state and structural type) a wide variety of physical and chemical properties can be conferred by varying the nature of the R group.

The carboxylate functional group has four lone pairs of electrons available for metal binding. These lone pairs subtend to an angle of 120° and are referred to as the *syn*- and *anti*-lone pairs (Figure 31). On the basis of stereoelectronic arguments it has been suggested that the *syn*-lone pairs are more basic than those in the *anti* position.

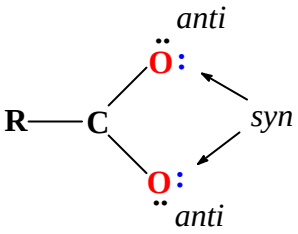



***Figure 31***: The carboxylate functional group[57]

The various coordination modes of the $RCO_2^-$ ligand are listed below:

(i) *Ionic.* The carboxylate salts of Na, K, Rb, and Cs have been shown to be ionic, with only coulombic interactions between the metal and the carboxylate ions.

(ii) *Monodentate.* In lithium acetate the metal is coordinated to one of the carboxylate oxygens.

(iii) *Bidentate Chelating*. Carboxylates may chelate either in a symmetrical mode, with both metal-oxygen bonds being of equal length, or in the asymmetrical mode (Figure 32(d)) where one metal-oxygen bond is shorter than the other. In zinc(II) acetate dihydrate the bonding mode of the acetate is symmetrical bidentate chelating, while in the mixed-ligand complex $[Zn(phen)_2(O_2CCH_3)][ClO_4]$ it is asymmetrical bidentate chelating. It has been found that the "bite angle" (i.e. the O-M-O angle) for a chelating carboxylate is *ca.* $60^o$ which, being fairly small, distorts the octahedral geometry of many metal complexes.

(iv) *Bidentate Bridging.* The planar carboxylate ion is ideally suited to the formation of complexes in which the carboxylate bridges two metal atoms (*Figure 32*(e-g)). The *syn-syn* mode is of particular interest since it is the type of bridging observed in the "lantern shaped" (paddlewheel) bimetallic carboxylates such as copper(II) acetate dihydrate. The *syn-syn* coordination mode is the only one which allows the ligand to bridge the short metal-metal bonds found in these binuclear complexes. Several binuclear ruthenium complexes[57] have carboxylate bridges in which the *anti-anti* mode of binding is found.

(v) *Monodentate Terminal Bridging*. This is one of the rarer binding modes (Figure 33(h)) and it has been suggested to be important biologically, and it is thought to act as an intermediate between other carboxylate bridging modes.[58]

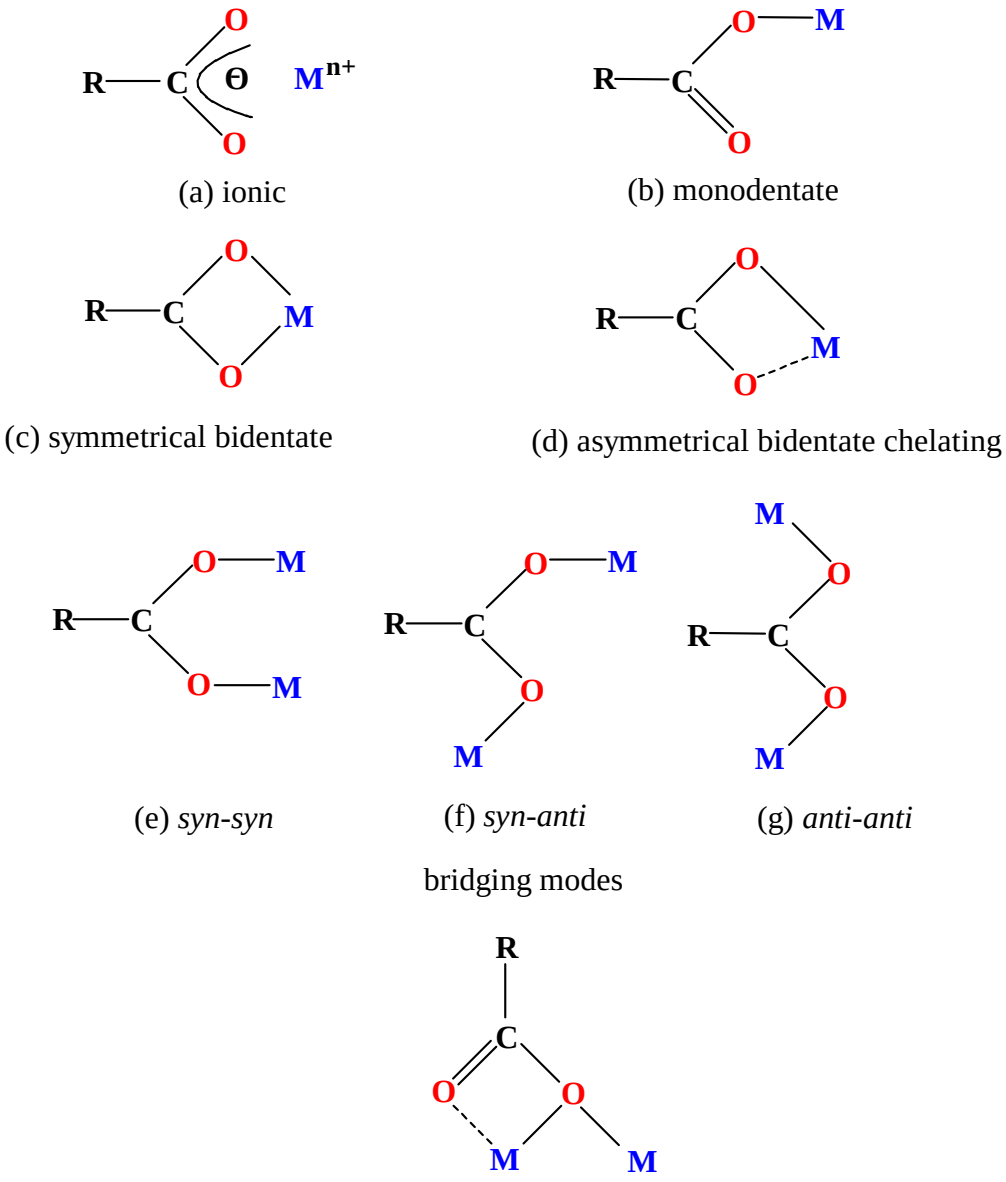


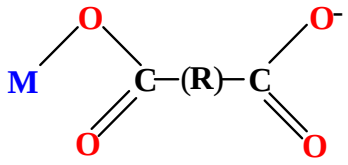

***Figure 32***: Coordination modes of monocarboxylic acids[58]

**I.9.2 Coordination modes of dicarboxylic acids**

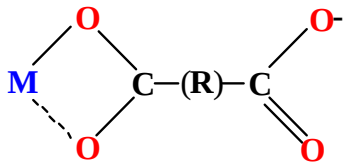
Dicarboxylic acids contain two -$CO_2^-$ functional groups, both of which can coordinate to a metal centre. This class of ligand can generate a myriad of structural motifs and has been chosen for this project to promote variation in structure and nuclearity. The unique versatility in the range of binding modes that dicarboxylic acids can adopt are broadly divided into three classes (Figure 32).[59]

(i) *Unidentate*. The simple dibasic acid, ethanedioic acid ($H_2OCCO_2H$) behaves as a unidentate ligand in the octahedral cobalt(III) complex $[Co(en)_2(X)(O_2CCO_2)]$ (en = ethylenediamine; X = $OH^-$ or halide).

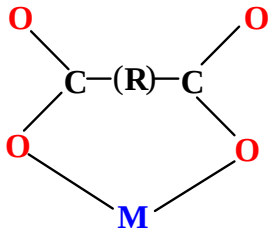
(ii) *Chelating*. The dicarboxylic acid group can chelate to the metal centre in a symmetrical or asymmetrical fashion, in which only one of the carboxylate groups is used for coordination. Small dibasic acids can utilise the close proximity of the two $RCO_2^-$ groups to act as chelating ligands where only one carboxylate oxygen from each of the $RCO_2^-$ groups binds the metal centre. An example in which the latter type of diacid coordination is present is the ethanedioic dicopper(II,II) complex $[tmen(H_2O)Cu(O_2CCO_2)Cu(H_2O)tmen](ClO_4)_2$(tmen=1,1,4,4tetramethylethylenediamine)




(a) unidentate




(b) symmetrical (or asymmetrical) using one carboxylate function




(**R** = alkyl, aryl)

(c) chelation using both carboxylate functional

***Figure 33***: Unidentate and chelating coordination modes for dicarboxylic acids.[59]

(iii) *Bridging* (Figure 34). This mode of binding is divided into three categories depending on the number of oxygen atoms that are complexed to the metal centre(s); bidentate (bridging *via* two oxygen atoms), tridentate (bridging *via* three oxygen atoms), and tetradentate (bridging *via* four oxygen atoms).

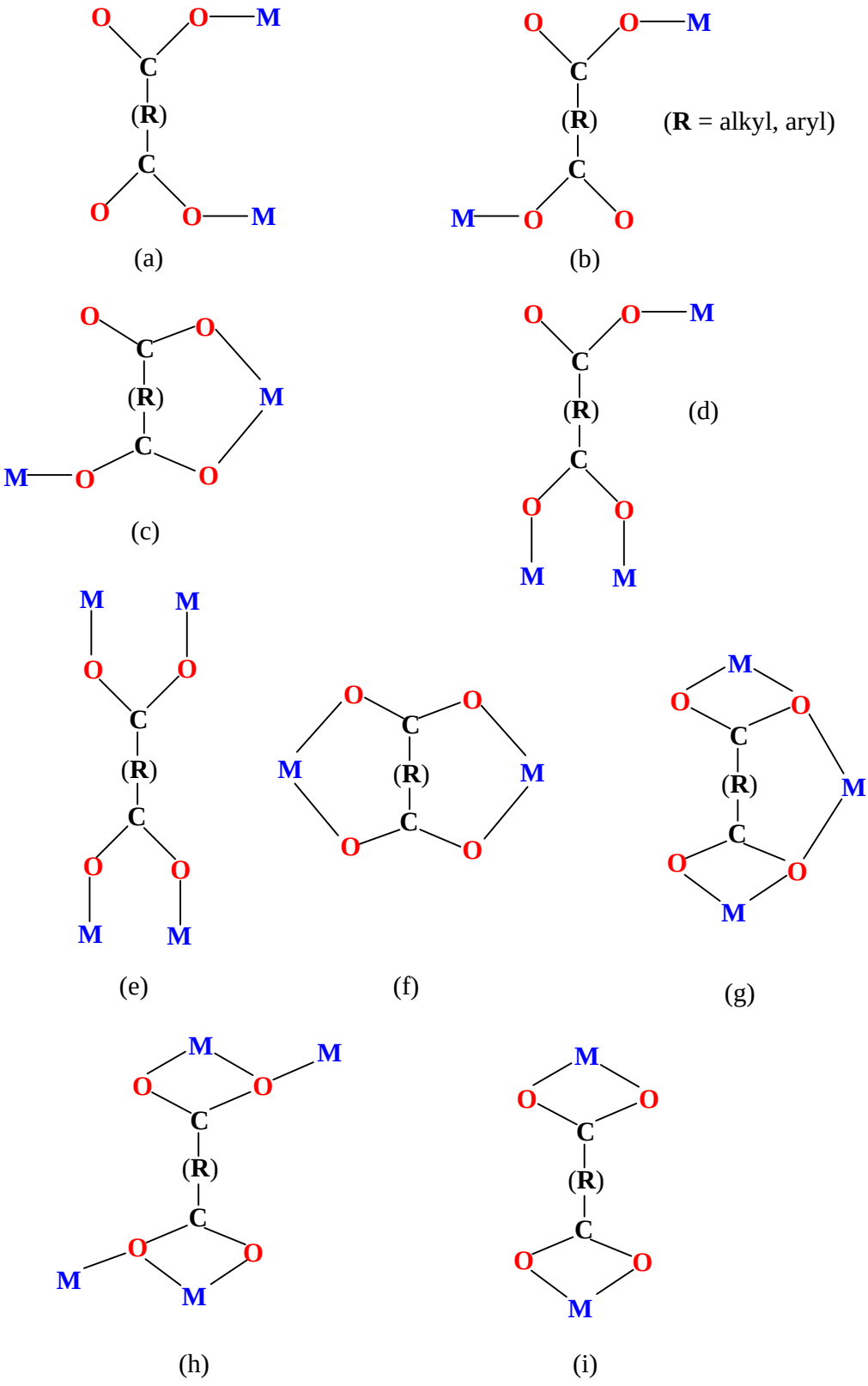



***Figure 34***: Mode of binding of dicarboxylate ligands[59]

### I.9.3 Infra-red spectra of carboxylate complexes

Infrared spectroscopy is a useful tool for assigning structural detail to carboxylate complexes. Upon complexation to a metal centre the $\nu_{C=O}$ absorption band of the $-CO_2H$ group in the free acid disappears, and two new bands relating to the antisymmetric ($\nu_{OCOasym}$) and symmetric ($\nu_{OCOsym}$) stretch appear around 1630-1585 $cm^{-1}$ and 1355-1330 $cm^{-1}$, respectively. The magnitude of separation between these two bands ($\Delta_{OCO}$ $cm^{-1}$) has been used as a diagnostic aid in the determination of the nature of the carboxylate coordination. $\Delta_{OCO} = (\nu_{OCOasym} - \nu_{OCOsym})$ $cm^{-1}$.

Deacon and Phillips[60] compiled guidelines for diagnosing the type of carboxylate coordination based on a metal complex's infra-red spectrum. Their findings were based on spectral data obtained for eighty four complexed acetates and halogenoacetates, and are summarised below:

(i) Ionic acetates, such as those of the alkali metals, have $\Delta_{OCO}$ values of *ca.* 165 $cm^{-1}$. For ionic trifluoroacetates the $\Delta_{OCO}$ value was *ca.* 235 $cm^{-1}$.

(ii) $\Delta_{OCO}$ values < 105 $cm^{-1}$ indicated symmetric chelating carboxylate coordination. Complexes in which the carboxylates bridge short metal-metal bonds may also show such low values.

(iii) $\Delta_{OCO}$ values substantially less than the ionic values (i.e. < 150 $cm^{-1}$ for acetates) indicate the presence of chelating or bridging carboxylate. Unidentate carboxylates which are strongly hydrogen-bonded ("pseudo-bridging") may also fall into this category.

(iv) For complexes with $\Delta_{OCO}$ values similar to those for ionic carboxylates the assignments were counted as untrustworthy. Deacon and Phillips found many examples of each type of coordination mode (except for symmetric chelating) in this category.

(v) Unidentate coordination was suggested for complexes where the $\Delta_{OCO}$ value was substantially greater than those for the ionic carboxylates (i.e. > 200 $cm^{-1}$ for acetates) An explanation for this difference in energy may be that the bonding of one oxygen to a metal, with the other oxygen free, increases the energy of the antisymmetric stretching mode.The above observations are summarised in Table 5**.** For a variety of reasons there can be many contradictions in the $\nu_{OCO}$ proposed band assignments. For example anion exchange from the alkali halide infra-red discs can occur, and there can also be uncertainties in locating exactly the $\nu_{OCOsym}$ stretching band.

***Table 5***: Infra-red spectral data ($\nu_{OCO}$) for coordinated acetate ligands[61]

| $\Delta_{OCO}(CH_3CO_2^-)$ ($cm^{-1}$) | Coordination mode |
|---|---|
| < 105 | symmetric chelating or short bridging |
| < 150 | chelating or bridging |
| *ca*. 165 | untrustworthy assignments |
| > 200 | Unidentate |

Caution should be applied to using these estimates as phenomena such as hydrogen bonding can significantly distort the $\Delta_{OCO}$ values.

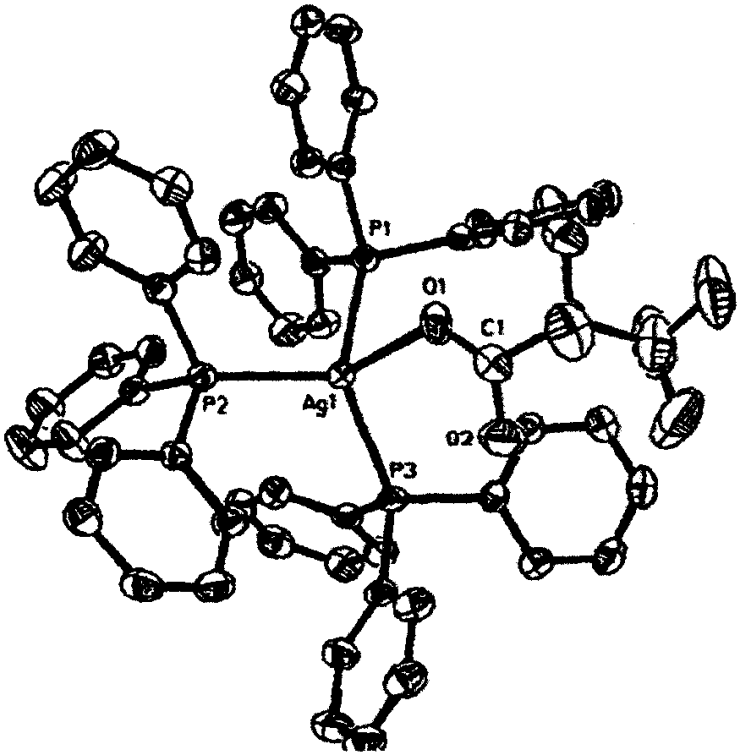
## I.10 SILVER(I) CARBOXYLATE COMPLEXES

### I.10.1 Silver(I) carboxylate complexes

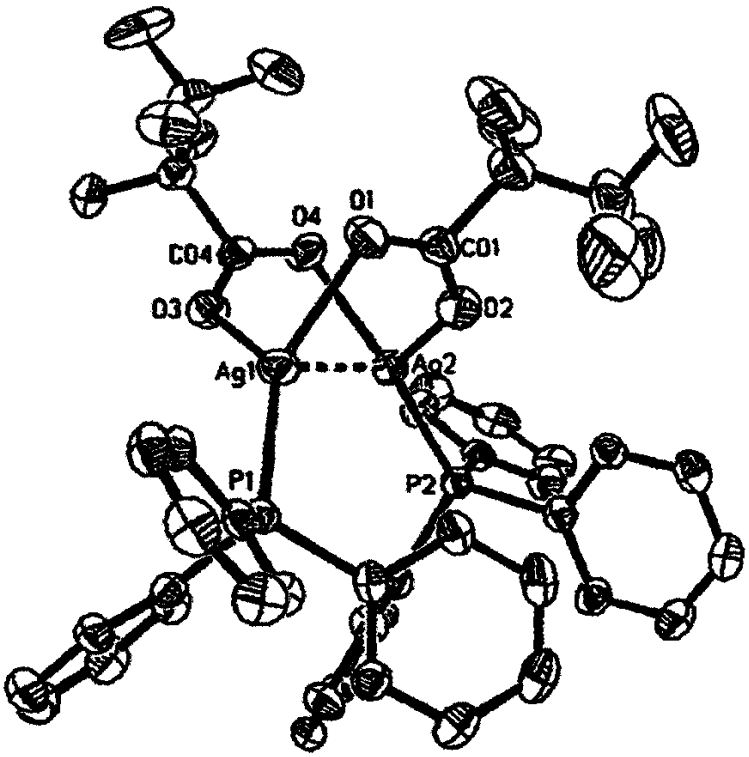
In the solid state, silver(I) carboxylates mostly form bridged dimers as in $[Ag_2(OOCC_6H_5)_2]$.[62] They also exhibit aggregation of these dimers into a ladder forming a polymeric network. Their poor solubility and light-sensitivity make their structural characterization difficult.

### I.10.2 Silver(I) carboxylate complexes with tertiary Phosphines

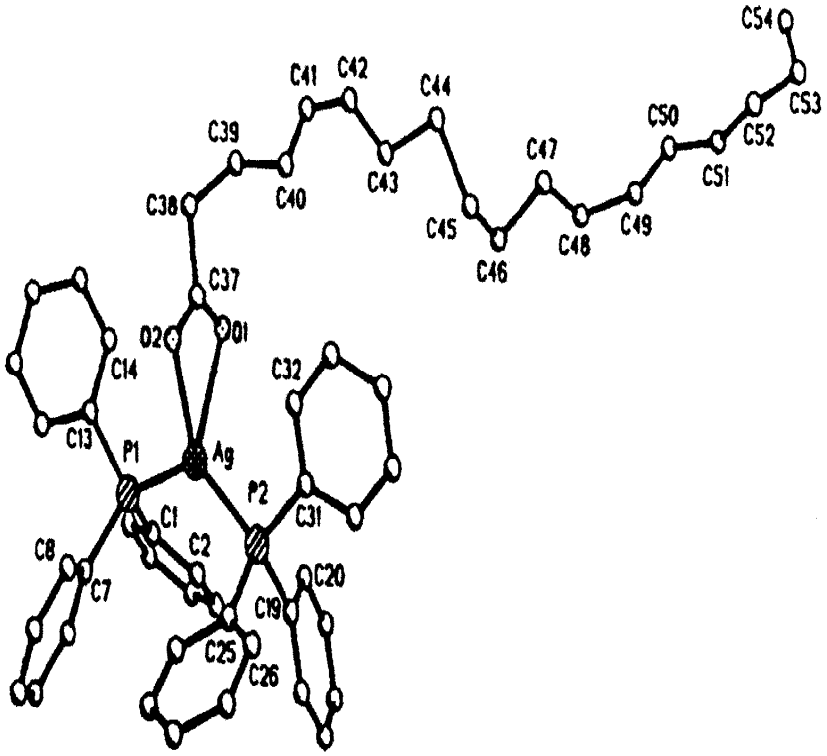
Reactions of silver(I) carboxylates with tertiary phosphines such as triphenylphosphine can lead to complexes which contain monodentate, bridging or chelating carboxylate ligands[62] and the number of phosphines attached to the silver can vary from one to three (*Figure 35*).




(a) Monodentate carboxylate




(b) Bridging carboxylate




(c) Chelating carboxylate

***Figure 35***: The structures of $[Ag(OOCC_2F_5)\{(PPh_3)_3\}]$ (a), $[Ag(OOCC_2F_5)(PPh_3)]_2$ (b) and $[Ag(OOC(CH_2)_{16}CH_3)(PPh_3)_2]$ (c)[62]

In 2005 Han *et al*[63] reported a series of triphenylphosphine co-ordinated silver α,β-unsaturated carboxylates of type $[Ag(O_2CR)(PPh_3)n$:n=1, R=$CH_3CH=CH$(2a), $(CH_3)_2C=CH$(2b), $CH_3CH_2CH=CH$(2c), $CH_3CH_2CH_2CH=CH$(2d), $PhCH=CH$(2e), $CH_2=CH$(2f), n=2, $CH_3CH=CH$(3a), $(CH_3)_2C=CH$(3b), $CH_3CH_2CH=CH$(3c), $CH_3CH_2CH_2CH=CH$(3d) were prepared by reaction of relative silver carboxylates (1a-1f) with triphenylphosphine in chloroform. These complexes were obtained in high yields and characterised by elemental analysis, $^1H$ NMR, $^{13}C$ NMR, $^{31}P$ NMR and IR spectroscopy. The molecular structure of $[Ag((O_2CCH=C(CH_3)_2))(PPh_3)_2]$ (3b) (Figure 36,37) shows that the senecioato ligand is chelated to the silver atom and generates, a distorted tetrahedron. Complex 3b exists as a monomer in crystal structure. The Silver atom is bonded to two oxygen atoms of the carboxyl at the same time. The angle P1-Ag1-P2 is 130.62$^o$. The angle of P1-Ag1-P2 is much more than the expected value of ideal tetrahedron geometry. This is due to the presence of six phenyl groups, which

creates a relatively more crowded environment around silver.

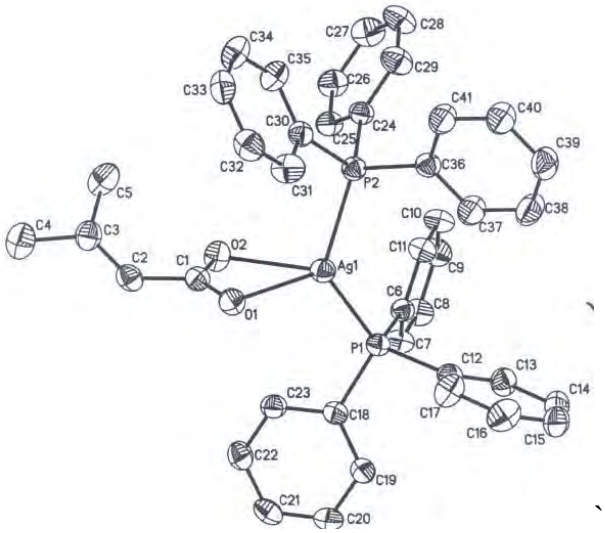



***Figure 36***: The crystal structure of $[Ag((O_2CCH=C(CH_3)_2))(PPh_3)_2]$[63]

The use of smaller phosphines such as $PMe_3$ leads to the formation of polymeric chain structures such as that of $[Ag(OOCC_2F_5)(PMe_3)]_n$

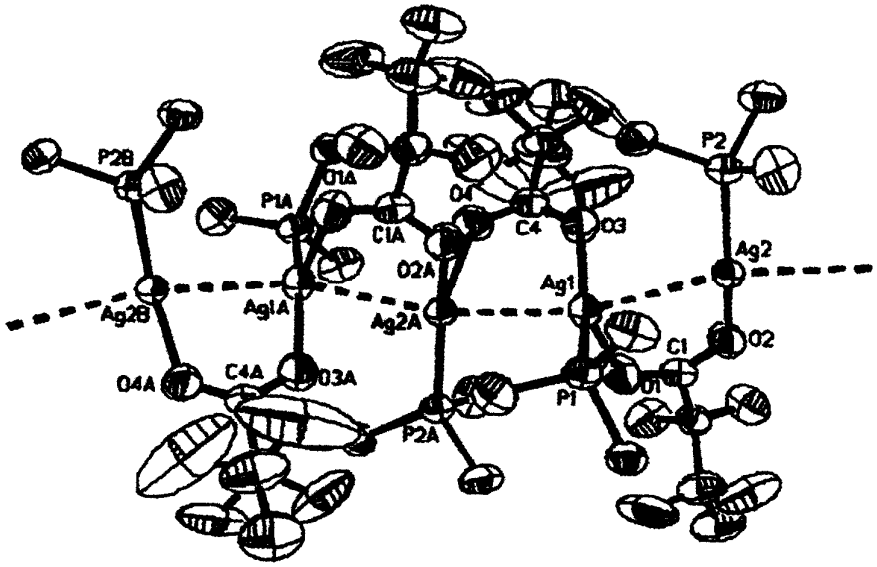
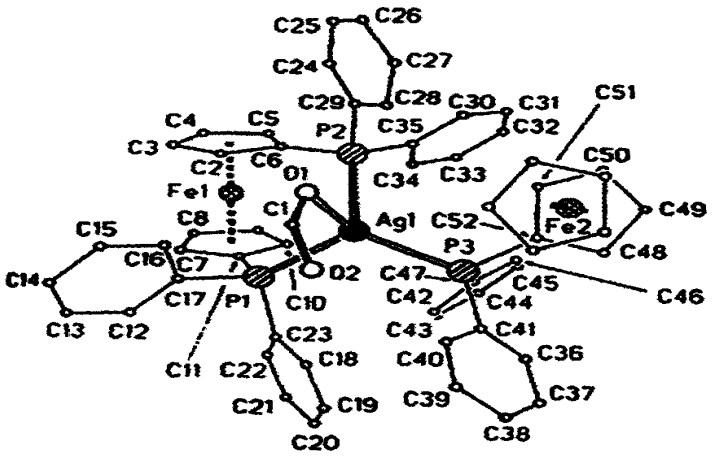



***Figure 37***: The chain-like structure of $[Ag(OOCC_2F_5)(PMe_3)]_n$[62]

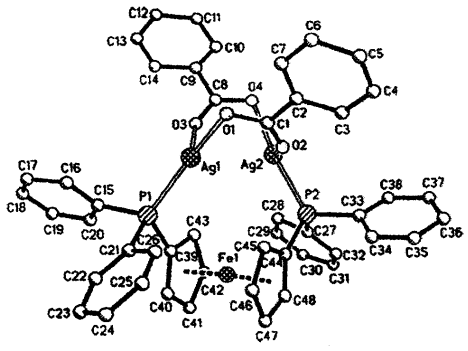
### I.10.3 Silver(I) carboxylate complexes with diphosphines

Diphosphines effectively stabilize Ag(I) carboxylate complexes through possible chelate and bridge binding, a feature which makes them attractive for generating

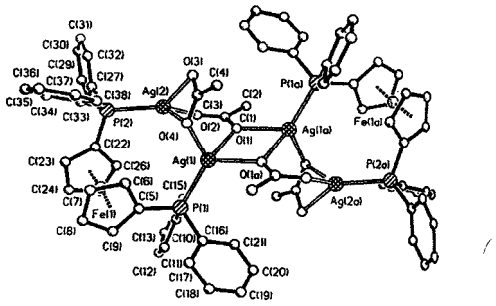
possible silver-based antimicrobial agents. These ligands stabilize silver(I) in its tetrahedral and trigonal planar geometries, and influence the nuclearity of the complexes. In comparison to monophosphines more complicated dinuclear, tetranuclear or polynuclear structures are observed. The Ag(I) carboxylate complexes with diphenylphosphinoferrocene (dppf) illustrate the variability of carboxylate bonding and nuclearity that can be achieved by this type of ligand when the type of carboxylate is varied (*Figure 38*) .




(a) Carboxylate = formate



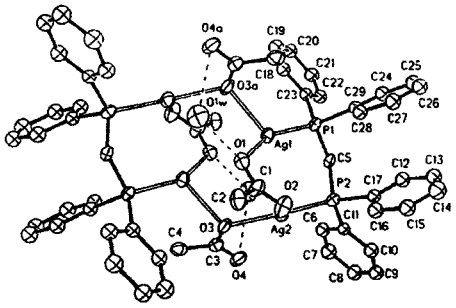
(b) Carboxylate = benzoate



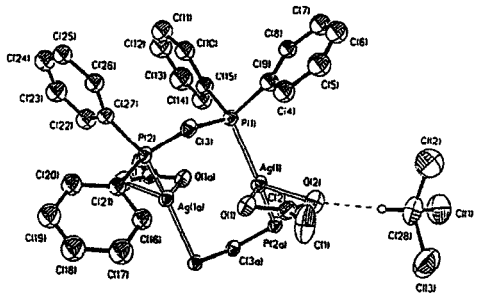
(c) Carboxylate = acetate

***Figure 38***: The variation in structures of $[Ag(OOCCH)_2(dppf)_3].2CH_2Cl_2$ (a) $[Ag_2(OOCC_6H_5)_2(\mu\text{-dppf})]$ (b) and $[Ag_4(OOCCH_3)_4(dppf)_2]$ (c)[62]

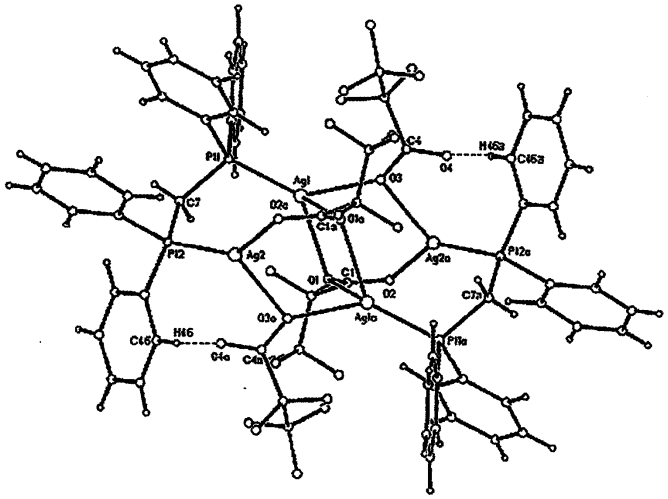
The versatility of carboxylates when used in conjunction with diphosphine ligands is also demonstrated for the stable diphenylphosphinomethane (dppm) complexes shown in Figure 39.



(a) carboxylate = acetate



(b) carboxylate = acetate



(c) carboxylate = pentaflouroacetate

***Figure 39***: The variation in structures of $[Ag_4(OOCCH_3)_4\{(\mu\text{-dppm})_2].2H_2O$ (a) $[Ag_2(OOCCH_3)_2\{(\mu\text{-dppm})_2].\ 2CHCl_3$ (b) and $[Ag_4(OOCC_2H_5)_4\{(\mu\text{-dppm})_2]$ (c)[62]

### I.10.4 Silver(I) dicarboxylate complexes with phosphines

Silver(I) dicarboxylate complexes with phosphine ligands are relatively scarce.[63] It has been proposed that silver(I) dicarboxylates form complexes with triphenylphosphines in which two silver atoms are bridged by the dicarboxylate ligand and each metal either has two or three phosphine attached to them (Figure40,41).[64]

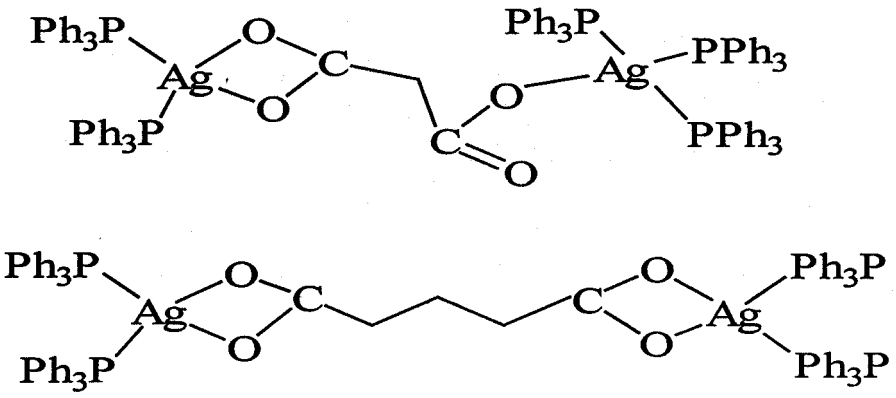



***Figure 40***: The proposed structure of silver(I)dicarboxylate triphenylphosphine complexes.[64]

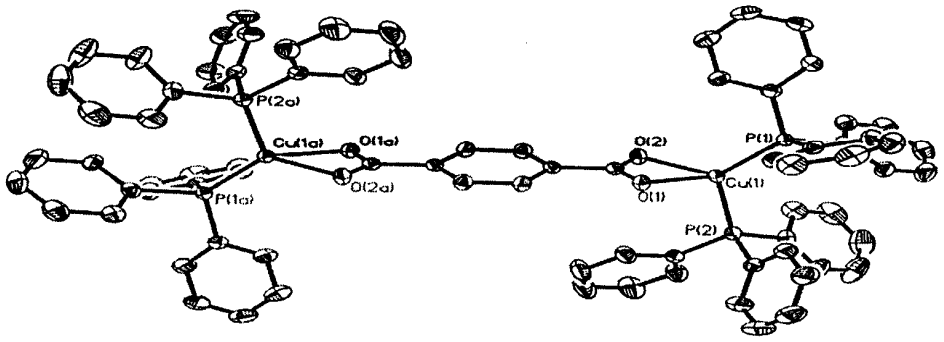



***Figure 41***: Structure of $[Cu_2(terph)(PPh_3)_4]$ ($terphH_2$ = terephthalic acid).[65]

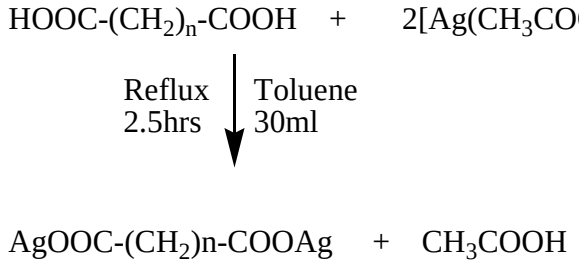
# RATIONALE

Silver(I) salts and simple silver(I) complexes are generally excellent antimicrobial agents. However it can be difficult to control the rate of silver ion release from these systems and they are often indiscriminate antimicrobials. A further problem arises from the fact that generally they are not photostable. The purpose of this study was to generate a series of light stable silver complexes as potential antimicrobial agents. The strategy employed the use of the aliphatic α, ω-dicarboxylic acids HOOC-$(CH_2)_n$-COOH (where n = 1-11) as primary ligands and counter ions with the intention of generating a series of novel compounds capable of releasing silver ions. These versatile dicarboxylate ligands have previously been shown, in this laboratory, to promote variations in structure and nuclearity (chain length dependent) when employed to make copper(II), manganese(II) and cobalt(II) complexes in the presence of auxiliary nitrogen donor ligands.[66] Because of the known instability of silver(I) carboxylate complexes the neutral donor phosphines $PPh_3$, dppm and dppe were employed as auxiliary ligands, as they are known to stabilize Ag (I) complexes and modify their silver ion release capabilities. It was hoped that the series of complexes generated using this approach would be stable, exhibit variation in structure and antimicrobial properties and that some interesting lead compounds with potential applications as novel antimicrobials would be identified.

# DISCUSSION

## D.1 SYNTHESIS AND CHARACTERISATION OF SILVER (I) DICARBOXYLATE COMPLEXES

The synthetic route to the silver dicarboxylate complexes $[Ag_2(prda)]$ **(1)**, $[Ag_2(bda)]$ **(2)**, $[Ag_2(pda)]$ **(3)**, $[Ag_2(hxda)]$ **(4)**, $[Ag_2(hpda)]$**(5)**, $[Ag_2(oda)]$ **(6)**, $[Ag_2(nda)]$ **(7)**, $[Ag_2(dda)]$ **(8)**, $[Ag_2(udda)]$ **(9)**, $[Ag_2(ddda)]$ **(10)** and $[Ag_2(uddca)]$ **(11)** is shown in ***Scheme 1***. The 11 complexes were generated by the reaction of $[Ag(CH_3COO)]$ with the relevant dicarboxylic acid.




n =1-11

***Scheme 1***: The synthetic route to the silver dicarboxylate complexes

The reaction was facilitated by removal of the condenser which removed the acetic acid byproduct and essentially drove the reaction forward.

Complex **1-11** were obtained as off-white powders. They were formulated as shown below in Table 6.

***Table 6***: Elementary Analysis of complexes **1-11**

| **Complex** | **Elementary Analysis** | | | |
|---|---|---|---|---|
| | **% Calculated** | | **% Found** | |
| | **C** | **H** | **C** | **H** |
| $[Ag_2(prda)]$ (**1**) | 11.34 | 0.63 | 11.32 | 0.64 |
| $[Ag_2(bda)]$ (**2**) | 14.48 | 1.22 | 14.22 | 1.68 |
| $[Ag_2(pda)]$ (**3**) | 17.36 | 1.75 | 17.22 | 1.6 |
| $[Ag_2(hxda)]$ (**4**) | 20.03 | 2.24 | 20.59 | 2.16 |
| $[Ag_2(hpda)]$ (**5**) | 22.49 | 2.7 | 22.43 | 2.26 |
| $Ag_2(oda)]$ (**6**) | 24.77 | 3.12 | 24.27 | 3.17 |
| $[Ag_2[(nda)]$ (**7**) | 26.89 | 3.51 | 26.39 | 3.01 |
| $[Ag_2(dda)]$ (**8**) | 28.87 | 3.88 | 28.11 | 3.5 |
| $[Ag_2(udda)]$ (**9**) | 28.87 | 3.66 | 28.34 | 3.84 |
| $[Ag_2(ddda)]$ (**10**) | 32.46 | 4.54 | 32.22 | 4.94 |
| $[Ag_2(uddca)]$ (**11**) | 34.09 | 4.84 | 34.44 | 4.77 |

***Table 7***: Characteristic IR bands ($cm^{-1}$, KBr discs) of the complexes **1**– **11**

| | (**1**) | (**2**) | (**3**) | (**4**) | (**5**) | (**6**) | (**7**) | (**8**) | (**9**) | (**10**) | (**11**) |
|---|---|---|---|---|---|---|---|---|---|---|---|
| ν(C-H)aliphatic | * | * | 2959 | 2925 | 2932 | 2930 | 2934 | 2930,2851 | 2930,2913,2846 | 2918 | 2848 |
| **Carboxylate band** | | | | | | | | | | | |
| $\nu_{(asym)(OCO)}$ | 1570 | 1566 | 1569 | 1564 | 1564 | 1566 | 1567 | 1567 | 1585 | 1568 | 1562 |
| $\nu_{(sym)(OCO)}$ | 1356 | 1410 | 1400 | 1409 | 1407 | 1410 | 1408 | 1408 | 1408 | 1409 | 1409 |
| $\Delta_{OCO}$ | 214 | 156 | 169 | 155 | 157 | 156 | 159 | 159 | 177 | 159 | 153 |

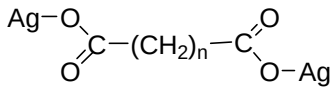
* Bands precluded by others in the infrared spectrum.

The IR spectra of complexes **1-11** are shown in the Appendix 1. Complexes **1-11** all have very similar IR spectra (Table 7) reflecting similar structural characteristics of this family of complexes. The important feature of the IR spectra of these complexes is the presence of the $\nu_{asym}$(OCO) and $\nu_{sym}$(OCO) bands which are indicative of the presence of the carboxylate ligand (Table 7). These bands are not split and therefore it is most likely that the two carboxylate groups are bound to the silver centres in the same mode for each dicarboxylate ligand. The $\Delta_{OCO}$ values for all complexes (153-214 $cm^{-1}$) are indicative of carboxylate groups bound to a metal centre in a monodentate coordination mode.[60] The presence of bands in the 2000-2950 $cm^{-1}$ of the IR spectra for these complexes further supports the presence of the dicarboxylate ligands and the increasing intensity of these bands results from the increase in fatty nature of the dicarboxylate ligands as the molecular weight of the ligands increases.

It is worth noting that early attempts to generate complexes **1-11** via the ligand exchange reaction between the diacids and the silver acetate (Scheme 1) yielded colourless powders which were difficult to formulate and had IR spectra that exhibited $\nu_{asym}$(OCO) and $\nu_{sym}$(OCO) groups that were split. Furthermore, the IR spectrum of silver acetate (Appendix1) is very similar to the spectra of complexes 1-11 in the carboxylate region. It transpired that these early products were mixtures of dicarboxylate and acetate silver salts and it was discovered that the critical element in the protocol for achieving pure samples of **1-11** was the removal of the condenser periodically during the reaction process. This allowed excess acetic acid to evolve out of the reaction vessel and yielded pure products.

Complexes **1-11** were found to have very limited solubility in the organic solvents. All attempts to obtain NMR spectra and conductivity of the complexes were unsuccessful due to the insolubility of the compounds.

A proposed structure that fits the physico-chemical properties of the complexes **1-11** is shown in Figure 42.




n= 1-11

***Figure 42***: A proposed structure of the complexes **1-11**

## D.2 SYNTHESIS AND CHARACTERISATION OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$) LIGAND

Complexes **1-11** were reacted with $PPh_3$ in 1:2.5, 1:4 and 1:6 molar ratios.

The synthetic route to the silver dicarboxylate triphenylphosphine complexes $[Ag_2(prda)(PPh_3)_3]$ (**12**), $[Ag_2(bda)(PPh_3)_3].C_7H_8$ (**13**), $[Ag_2(pda)(PPh_3)_3].2H_2O$ (**14**), $[Ag(hxdaH)(PPh_3)_2]$ (**15**)$\{Ag(hpdaH)(PPh_3)_3.2H_2O\}_n$(**16**),$\{Ag_2(oda)(PPh_3)_3.2H_2O\}_n$ (**17**), $[Ag(ndaH)(PPh_3)_2]$(**18**), $[Ag_2(dda)(PPh_3)_4].2C_7H_8$(**19**), $[Ag_2(udda)(PPh_3)_2]$ (**20**), $[Ag(ddda)(PPh_3)_3]$ (**21**) and $[Ag(uddcaH)(PPh_3)_2]$ (**22**) is shown in Scheme 2. Complex **12-22** resulted from the reaction of the relevant Ag(I) dicarboxylate salt with 2.5 equivalents of $PPh_3$ as shown in Scheme 2**.**

$$[Ag_2(OOC\text{-}(CH_2)_n\text{-}COO)] \quad + \quad 2.5PPh_3$$

Reflux 2.5hrs | Toluene 30ml ↓

$$[Ag_x(OOC\text{-}(CH_2)_n\text{-}COOH_y)(PPh_3)_z]$$

n=1-11

x = 1or 2, y = 0 or 1 and z = 2 – 4

***Scheme 2***: The synthetic route to the silver dicarboxylate triphenylphosphine complexes

Complex **12** to **21** were obtained as off-white powders. Complex 22 was obtained as colourless crystals. They were formulated as shown below in Table 8.

***Table 8***: Elementary Analysis of complexes **12** to **22**

| Complex | Elementary Analysis | | | | | |
|---|---|---|---|---|---|---|
| | % Calculated | | | % Found | | |
| | C | H | P | C | H | P |
| $[Ag(prdaH)(PPh_3)_2].C_7H_8$ (**12**) | 63.69 | 4.52 | 8.42 | 64.49 | 4.61 | 7.22 |
| $[Ag_2(bda)(PPh_3)_3].C_7H_8$ (**13**) | 64.48 | 4.74 | 7.67 | 64.98 | 4.98 | 7.89 |
| $[Ag_2(pda)(PPh_3)_3].2H_2O$ (**14**) | 60.63 | 4.74 | 7.95 | 60.51 | 4.43 | 7.86 |
| $[Ag_2(hxda)(PPh_3)_2]$ (**15**) | 57.04 | 4.33 | 7.00 | 57.04 | 4.30 | 6.43 |
| $[Ag_2(hpda)(PPh_3)_2].2H_2O$ (**16**) | 61.12 | 5.13 | 7.75 | 61.60 | 4.87 | 7.27 |
| $\{[Ag_2(oda)(PPh_3)_3].2H_2O\}_n$ (**17**) | 61.40 | 5.24 | 7.66 | 61.02 | 5.07 | 7.44 |
| $[Ag(ndaH)PPh_3)_2]$ (**18**) | 65.94 | 5.53 | 7.56 | 66.95 | 5.16 | 8.50 |
| $[Ag_2(dda)(PPh_3)_4].2C_7H_8$ (**19**) | 69.82 | 5.74 | 7.50 | 69.23 | 5.21 | 7.58 |
| $[Ag_2(udda)(PPh_3)_2]$ (**20**) | 59.01 | 5.27 | 6.48 | 59.46 | 5.00 | 6.63 |
| $[Ag_2(ddda)(PPh_3)_3]$ (**21**) | 64.40 | 5.33 | 7.55 | 64.55 | 5.53 | 7.43 |
| $[Ag(uddcaH)(PPh_3)_2]$ (**22**) | 67.20 | 6.10 | 7.07 | 66.83 | 6.02 | 7.31 |

Complexes **12-22** formulate in three categories (i) $\{Ag_2(O_2C\text{-}(CH_2)_nCO_2)(PPh_3)_3\}_n$ ; (ii)$[Ag(O_2C\text{-}(CH_2)_n\text{-}COOH)(PPh_3)_2]$; and (iii) $\{Ag_2(O_2C\text{-}(CH_2)_n\text{-}CO_2(PPh_3)_4\}_n$. Complexes **12, 13, 14, 17** and **21** fall into category (i), complexs **15, 16, 18** and **22** fall into category (ii) and complexes **19** and **20** formulate as shown in category (iii). Furthermore, early attempts to react the $PPh_3$ with complex 1-11 in a 2.5 : 1 ratio were flawed as a result of using the mixtures of $[Ag(CH_3COO)]$ and $[Ag_2(dicarboxylate)]$ inadvertently. This point was demonstrated when crystals from the intial reaction of 2.5 $PPh_3$ and what was believed to be $[Ag_2(O_2C\text{-}(CH_2)_5\text{-}CO_2)]$ were isolated. These turned out to be a co-crystallised product ( ie 2 complexes present in one crystal lattice). The crystal comprised two components $[Ag(PPh_3)_2(CH_3COO)]$ and $\{Ag(hpdaH)(PPh_3)_2\}_n$.These structures are shown in Figures 43, 44 and 45 and selected bond lengths and angles for them are listed in Tables 9 and 10.

The $[Ag(PPh_3)_2(CH_3COO)]$ (Figure 44) component is reasonably well-behaved and does not show any very striking interactions with the other species present (though there are many weak interactions involving the phenyl groups- see (Figure 45). The other silver species forms a $\{Ag(PPh_3)_2(OOC(CH_2)_5COOH)\}_n$ polymeric chain running

parallel to the b axis in which the silver ions are bridged by $OOC(CH_2)_5COOH$ anions, Figure 45. This link is reinforced by H-bonding between the chains. There is some disorder in this component – in which the silver ion and one of the $PPh_3$ groups take up alternate positions.[67] Since the minor component is quite small (estimated 15%) only the Ag and P positions have been modelled. A second data set shows this disorder more clearly.The toluene solvate is disordered and modelled with equal occupancy of two overlapping sites.

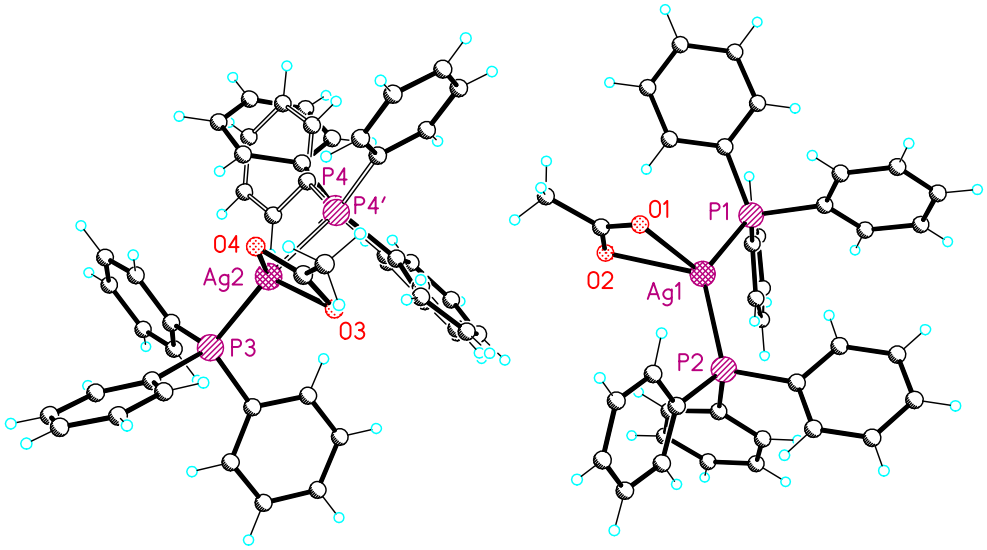



***Figure 43***: Structure of the $[Ag(PPh_3)_2(CH_3COO)]$ component of the co-crystallised product from the reaction of impure $[Ag_2(hpda)]$ complex with $PPh_3$

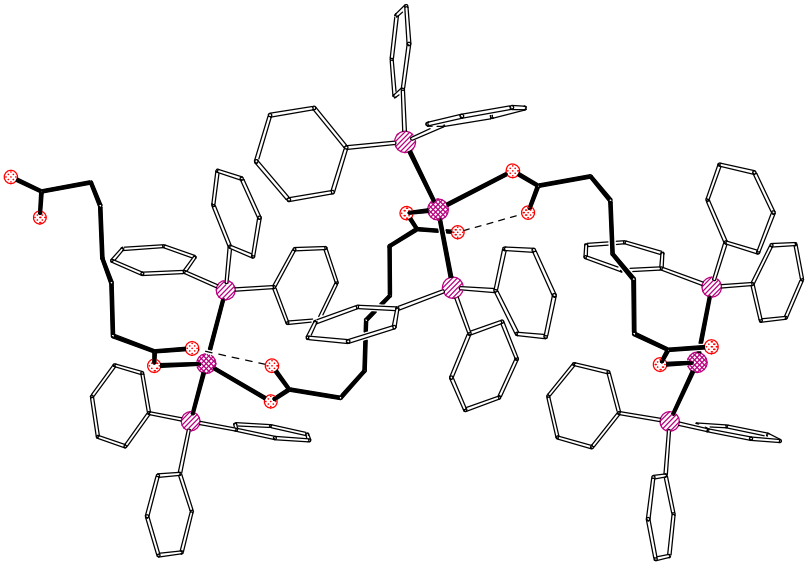


***Figure 44***: The polymeric structure of {Ag(hpdaH)($PPh_3$)$_2$}n component of the co-crystallised product from the reaction of the impure [$Ag_2$(hpda)] complex with $PPh_3$

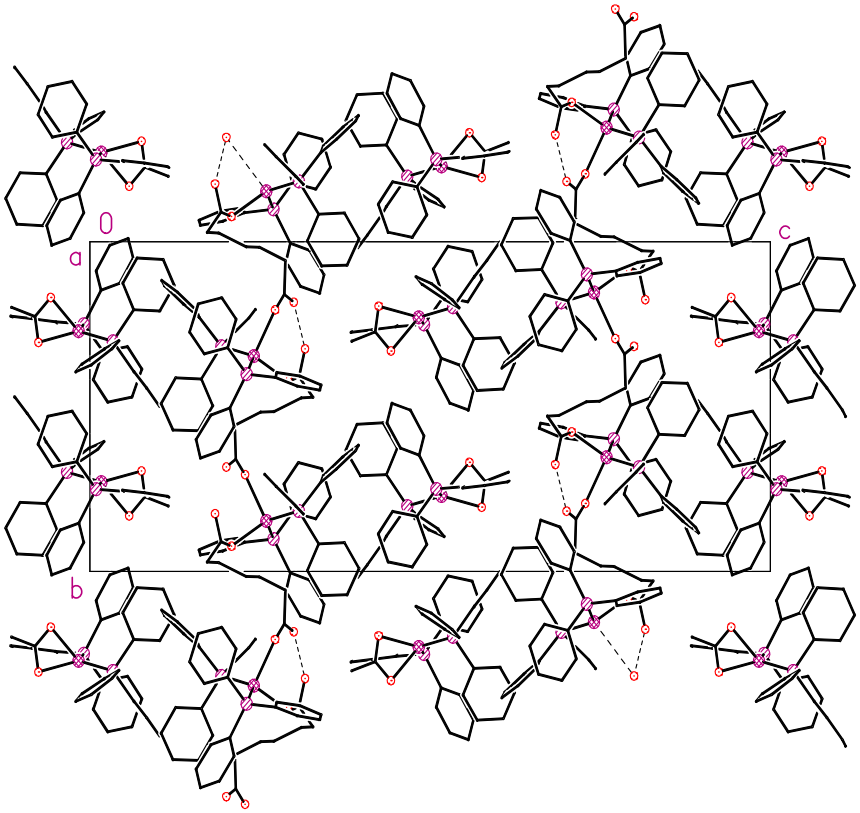



***Figure 45***: Packing diagram for the co-crystallised [Ag($PPh_3$)$_2$($CH_3COO$)]/{Ag(hpdaH)($PPh_3$)$_2$}$_n$ product.

***Table 9***: Selected bond lengths [Å] and angles [°] around the silver centres in **[**$Ag(PPh_3)_2(OAc)$] component of the co-crystallised product from the reaction of impure [$Ag_2$(hpda)] complex with $PPh_3$

| Complex (**16A**) | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(2) | 2.417(2) |
| Ag(1)-P(2) | 2.4232(8) |
| Ag(1)-P(1) | 2.4394(8) |
| Ag(1)-O(1) | 2.441(2) |
| Bond angles ° | |
| O(2)-Ag(1)-P(2) | 115.91(6) |
| O(2)-Ag(1)-P(1) | 105.10(6) |
| P(2)-Ag(1)-P(1) | 129.58(3) |
| O(2)-Ag(1)-O(1) | 53.99(7) |
| P(2)-Ag(1)-O(1) | 112.18(6) |
| P(1)-Ag(1)-O(1) | 115.34(6) |

***Table 10***: Selected bond lengths [Å] and angles [°] around the silver centres in the$\{Ag(hpdaH)(PPh_3)_2\}_{n1}$ component of the co-crystallised product from the reaction of impure $[Ag_2(hpda)]$ complex with $PPh_3$

| Complex (**16**) | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.386(9) |
| Ag(1)-P(1) | 2.419(2) |
| Ag(1)-P(2) | 2.4524(19) |
| Ag(1)-O(3)#1 | 2.500(9) |
| Ag(1')-P(2) | 2.320(5) |
| Ag(1')-P(1') | 2.530(11) |
| Bond angles ° | |
| O(1)-Ag(1)-P(1) | 111.0(3) |
| O(1)-Ag(1)-P(2) | 109.6(2) |
| P(1)-Ag(1)-P(2) | 125.86(7) |
| O(1)-Ag(1)-O(3)#1 | 100.4(5) |
| P(1)-Ag(1)-O(3)#1 | 110.1(3) |
| P(2)-Ag(1)-O(3)#1 | 95.9(2) |

When pure $[Ag_2(hpda)]$ was reacted with 2.5 equivalents of $PPh_3$ the complex $[Ag_2(hpda)(PPh_3)_2].2H_2O$ **16** was isolated.

Crystals of **17** suitable for X-ray structural analysis were obtained when the mother liquor was left to stand for several weeks. The structure of **17** is shown in Figures 45 and 46 and selected bond lengths and angles are listed in Table 11.

The polymeric structure results from the bridging nature of the dicarboxylate anions (Figure 46). The repeating unit comprises two silver ions linked by two oxygen bridges, Note that the metal ions have different coordination numbers.[68] Quite likely some of this is driven by the packing interactions between the phenyl groups (Figure 47). There is possibly a weak interaction between Ag2 and the second carboxylate oxygen. The

Ag1-Ag2 distance is 3.7254(2) Å. and therefore no significant Ag…..Ag interaction is found in the complex.

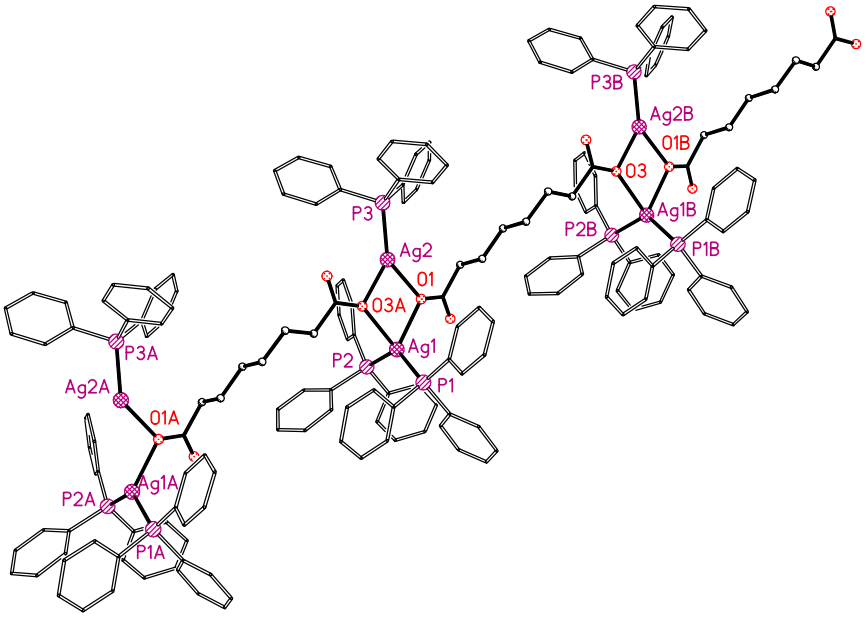



***Figure 46***: The polymeric structure of $\{Ag_2(oda)(PPh_3)_3\}_n$ **(17)**

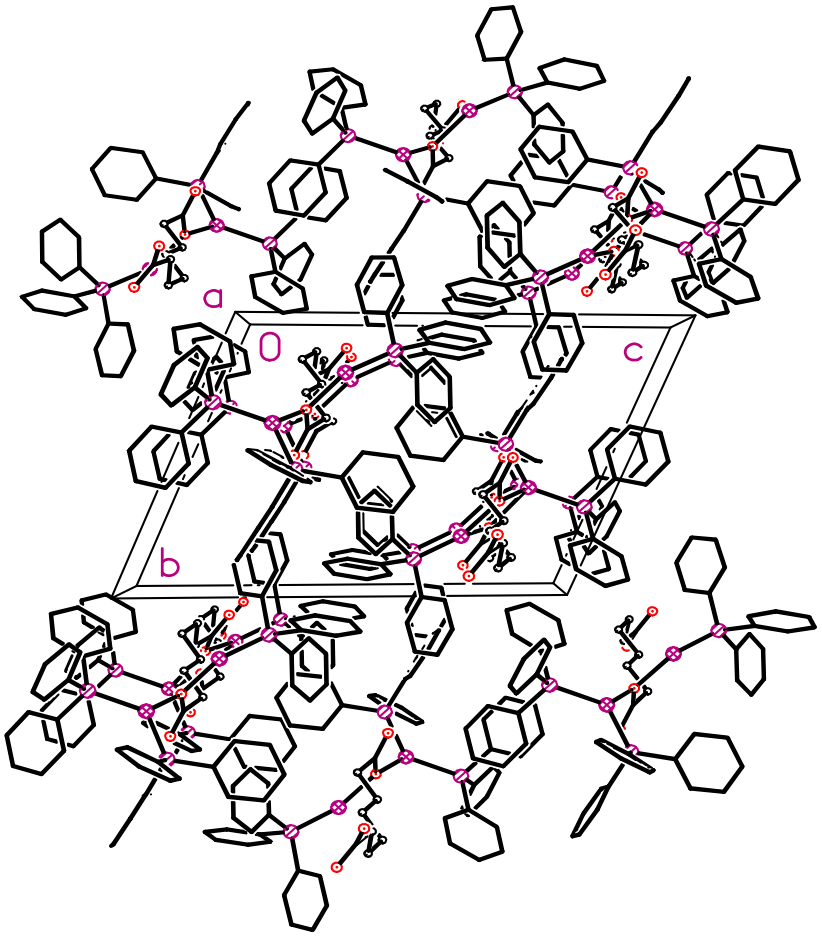



***Figure 47***: Packing diagram for $\{Ag_2(oda)(PPh_3)_3\}_n$ **(17)**

***Table 11***: Selected bond lengths [Å] and angles [°] around the silver centres in $\{Ag_2(oda)(PPh_3)_3\}_n$ **(17)**

| Complex **17** | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.3214(12) |
| Ag(1)-P(1) | 2.4245(5) |
| Ag(1)-P(2) | 2.4293(4) |
| Ag(1)-O(3)#1 | 2.4680(13) |
| Ag(2)-O(3)#1 | 2.2205(13) |
| Ag(2)-O(1) | 2.2726(12) |
| Ag(2)-P(3) | 2.3314(4) |
| Bond angles ° | |
| O(1)-Ag(1)-P(1) | 112.70(4) |
| O(1)-Ag(1)-P(2) | 113.23(4) |
| P(1)-Ag(1)-P(2) | 129.402(15) |
| O(1)-Ag(1)-O(3)#1 | 70.41(4) |
| P(1)-Ag(1)-O(3)#1 | 109.53(4) |
| P(2)-Ag(1)-O(3)#1 | 104.81(4) |
| O(3)#1-Ag(2)-O(1) | 75.91(4) |
| O(3)#1-Ag(2)-P(3) | 145.61(4) |
| O(1)-Ag(2)-P(3) | 137.50(3) |

Crystals of **18** suitable for X-ray structural analysis were obtained when the mother liquor was left to stand for several weeks. The structure of **18** is shown in Figures 48 and 49 and selected bond lengths and angles are listed in Tables 12 and 13.

The carboxylic acid is mono-deprotonated; the carboxylate end acts as a bidentate ligand to the silver while the carboxylic acid end is linked to a neighbouring complex by hydrogen bonding (Figure 49).[69] The result is H-bonded chains running through the structure parallel to the b axis.

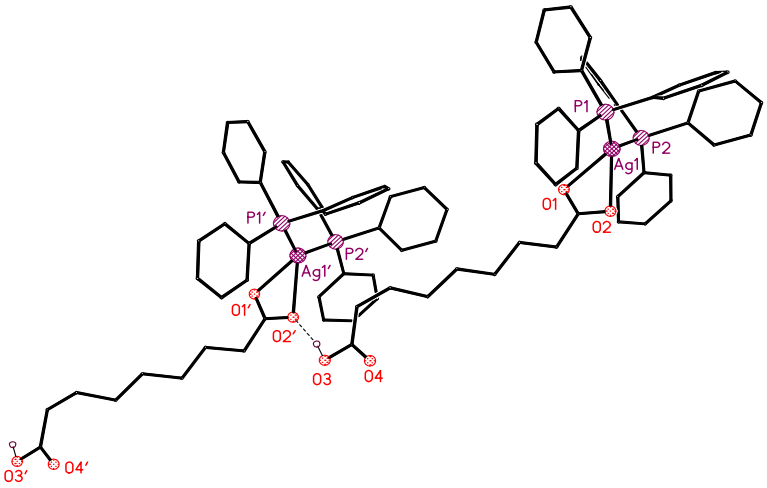



***Figure 48***: The structure of $[Ag(ndaH)(PPh_3)_2]$ **(18)**

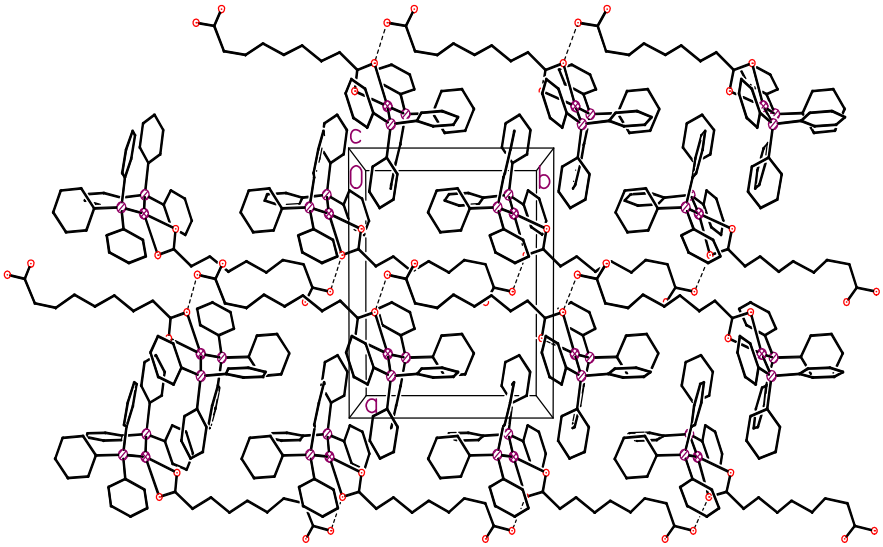



***Figure 49***: Packing diagram for $[Ag(ndaH)(PPh_3)_2]$ **(18)**

***Table 12***: Selected bond lengths [Å] and angles [°] around the silver centres in [Ag(ndaH)($PPh_3$)$_2$] (**18**)

| Complex 18 | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.3736(14) |
| Ag(1)-P(2) | 2.4255(5) |
| Ag(1)-P(1) | 2.4319(6) |
| Ag(1)-O(2) | 2.5409(15) |
| Bond angles ° | |
| O(1)-Ag(1)-P(2) | 109.75(4) |
| O(1)-Ag(1)-P(1) | 114.44(4) |
| P(2)-Ag(1)-P(1) | 131.221(19) |
| O(1)-Ag(1)-O(2) | 53.19(5) |
| P(2)-Ag(1)-O(2) | 118.08(4) |
| P(1)-Ag(1)-O(2) | 104.62(4) |

***Table 13***: Hydrogen bonds for [Ag(ndaH)($PPh_3$)$_2$] **(18)**

[Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(3)-H(3)...O(2)#1 | 0.95 | 1.70 | 2.627(2) | 166.1 |

Symmetry transformations used to generate equivalent atoms: #1 x,y+1,z

Crystals of **22** suitable for X-ray structural analysis were obtained when the mother liquor was left to stand for several weeks. The structure of **22** is shown in Figures 50 and 51 and selected bond lengths and angles are listed in Table 14 and 15.

Each silver ion is coordinated to two $PPh_3$ ligands and to a bidentate carboxylate group. The second acid group of the diacid is not deprotonated but hydrogen-bonded to a neighbouring coordinated carboxylate (under symmetry operation -x+1,-y+1,-z+1).[70] This results in the formation of H-bonded centrosymmetric dimers. There is a slight disorder in part of the alkyl chain modelled as 90:10 occupancy of two related positions.

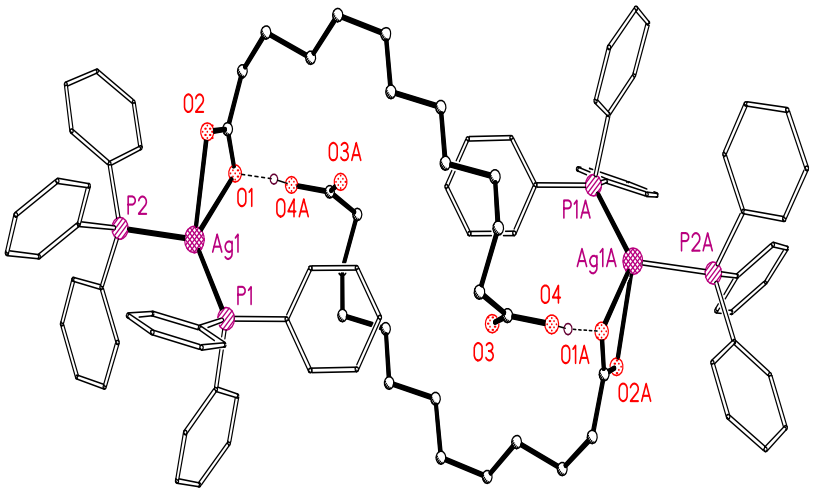



***Figure 50***: The structure of [Ag(uddcaH)($PPh_3$)$_2$] (**22**) showing the hydrogen bonding between molecules

It is worth noting the significant difference in the way the dicarboxylate group behaves in **22** compared to those in complex **18.** The –$(CH_2)_n$- chain length in the dicarboxylate acid has a profound effect on the way the complexes pack into the crystal.

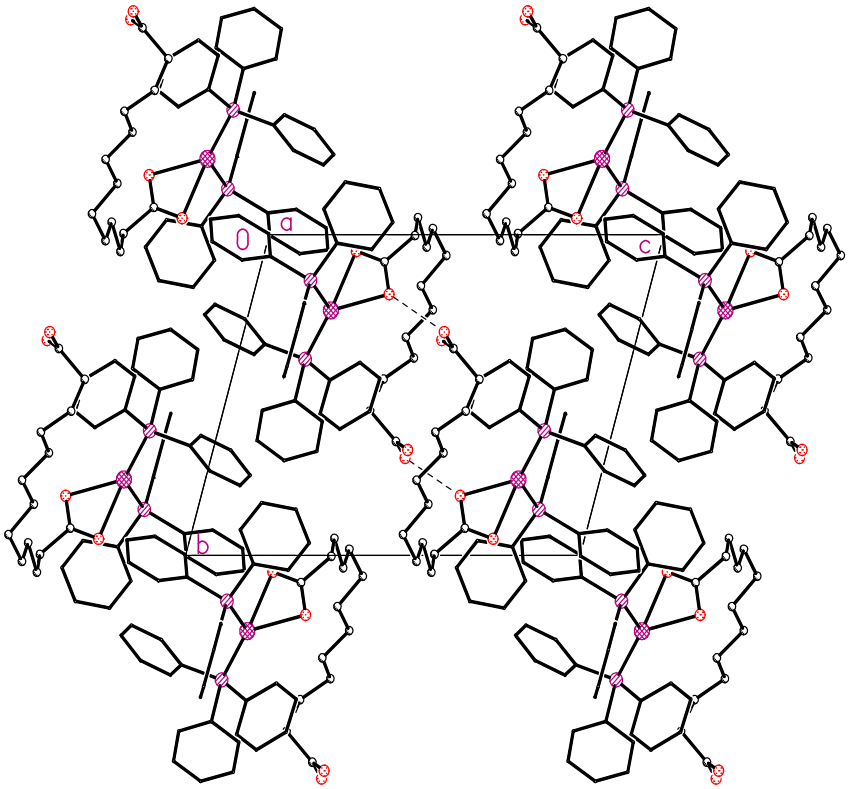



***Figure 51***: Packing diagram for [Ag(uddcaH)($PPh_3$)$_2$] **(22)**

***Table 14***: Selected bond lengths [Å] and angles [°] around the silver centres in [Ag(uddcaH)($PPh_3$)$_2$] **(22)**

| Complex **(**22**)** | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.3697(15) |
| Ag(1)-P(1) | 2.3958(6) |
| Ag(1)-P(2) | 2.4500(6) |
| 1Ag(1)-O(2) | 2.5095(16) |
| Bond angles ° | |
| O(1)-Ag(1)-P(1) | 124.66(4) |
| O(1)-Ag(1)-P(2) | 103.77(4) |
| P(1)-Ag(1)-P(2) | 129.48(2) |
| O(1)-Ag(1)-O(2) | 53.42(5) |
| P(1)-Ag(1)-O(2) | 122.17(4) |
| P(2)-Ag(1)-O(2) | 96.63(5) |

***Table 15***: Hydrogen bonds for [Ag(uddcaH)($PPh_3$)$_2$] **(22)** [Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(4)-H(4)...O(1)#1 | 0.83(3) | 1.72(3) | 2.553(2) | 175(3) |

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1

The IR spectra of complexes **12-22** are shown in the Appendix 1.The IR spectral data that are indicative of the structural features of the complexes **12-22** are shown in Table 14. The spectra of the complexes **13**, **14**, **15** and **21** are all similar to that of complex **17** and therefore it is likely that they share a similar structure. Complex **12** formulates as having one Ag, two $PPh_3$ groups and a mono deprotonated dicarboxylic acid ligand and

the IR spectral data support a structure similar to those of the structurally characterised complexes **18** and **22**.[60] Furthermore, the presence of the COOH group in **12**, **18** and **22** is supported by C=O stretches in their IR spectra (Table16).

Complexes **19** and **20** formulate as $[Ag_2(dicarboxylate)(PPh_3)_4]$ and the IR spectral features are the same for both complexes. A structure that fit's the physico-chemical properties of **19** and **20** is shown in Figure 52.

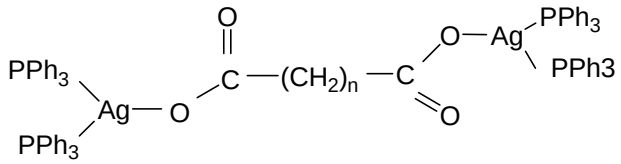



***Figure 52***: Possible structure for complexes **19** and **20**

Complexes **12-22** were found to have very limited solubility in organic solvents and all attempts to obtain NMR spectra and the conductivity of the complexes were unsuccessful.

***Table 16***: Characteristic IR bands ($cm^{-1}$, KBr discs) of the complexes (**12)**-(**22**) along with the free ligand

| | $PPh_3$ | (**12**) | (**13**) | (**14**) | (**15**) | (**16**) | (**17**) | (**18**) | (**19**) | (**20**) | (**21**) | (**22**) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ν (C-H) aromatic | | 3053 | 3053 | 3052 | 3049 | 3052 | 3053 | 3053.22 | * | 3051 | 3051 | 3054 |
| ν (C-H) aliphatic | | * | * | 2962,2920 | 2934 | 2941 | 2930,2851 | 2938 | 2921 | 2922 | 2924,2851 | 2922 |
| ν (C=O) | | 1731 | | | | | | 1736 | | | | 1703 |
| **Carboxylate** | | | | | | | | | | | | |
| **band** | | 1598 | 1549 | 1549 | 1620 | 1548 | 1593 | 1546 | 1478 | 1547 | 1560 | 1562 |
| ν (asym)(OCO) | | 1370 | 1393 | 1393 | 1366 | 1400 | 1407 | 1403 | 1433 | 1397 | 1406 | 1402 |
| ν (sym)(OCO) | | 228 | 156 | 156 | 254 | 148 | 186 | 143 | 45 | 150 | 154 | 160 |
| Δ OCO | | | | | | | | | | | | |
| **Phosphine bands** | | | | | | | | | | | | |
| **νC-P** | 744 | | | | | | | | | | | |
| νasym | 692 | 753.18 | 745.25 | 745.26 | 746.58 | 748.28 | 746.56 | 746 | 752 | 745 | 745 | 745 |
| νsym | | 694.60 | 693.43 | 693.62 | 693.08 | 694.52 | 693.60 | 694 | 693.85 | 694.55 | 695 | 694 |

* Bands precluded by others in the infrared spectrum.

## D.3 SYNTHESIS AND CHARACTERISATION OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$)

The synthetic route to the silver dicarboxylate triphenylphosphine complexes $[Ag_2(prda)(PPh_3)_3].H_2O$ (**23**), $[Ag_2(bda)(PPh_3)_4]$ (**24**), $[Ag_2(pda)(PPh_3)_4]$ (**25**), $[Ag(hxda)(PPh_3)_4]$ $.2H_2O$(**26**), $[Ag_2(hpda)(PPh_3)_4].C_7H_8$(**27**), $[Ag_2(oda)(PPh_3)_4].2.C_7H_8$(**28**), $[Ag_2(oda)(PPh_3)_4]$ (**28A**), $[Ag_2(ndaH)(PPh_3)_4].2H_2O$ (**29**), $[Ag_2(dda)(PPh_3)_4].H_2O$ (**30**), $[Ag_2$ (udda) $(PPh_3)_3]$ (**31**), $[Ag_2$ (udda) $(PPh_3)_4]$(**31A**)**,** $[Ag(ddda)(PPh_3)_3]_n$ **(32)** and $Ag(PPh_3)_2(HOOC(CH_2)_9COO)$**(33)** is shown in Scheme 3**.**

Complex **23-33** resulted from the reaction of the relevant Ag(I)dicarboxylate salt with 4 equivalents of $PPh_3$ as shown in Scheme 3

$$[Ag_2(OOC\text{-}(CH_2)_n\text{-}COO)] \quad + \quad 4PPh_3$$

Reflux 2.5hrs; Toluene 30ml ↓

$$[Ag_x(OOC\text{-}(CH_2)_n\text{-}COOH_y)(PPh_3)_z]$$

n=1- 11

X=1or2, y = 0 or 1 and z = 2-4

***Scheme 3***: The synthetic route to the silver dicarboxylate triphenylphosphine complexes

Complex **23** to **33** were obtained as off-white powders. They were formulated as shown below in Table 17.

***Table 17***: Elementary Analysis of complexes **23** to **33**

| Complex | Elementary Analysis | | | | | |
|---|---|---|---|---|---|---|
| | % Calculated | | | % Found | | |
| | C | H | P | C | H | P |
| $[Ag_2(prda)(PPh_3)_3].H_2O$ (**23**) | 60.98 | 4.4 | 8.28 | 60.95 | 4.29 | 8.18 |
| $[Ag_2(bda)(PPh_3)_4]$ (**24**) | 66.1 | 4.67 | 8.97 | 66.05 | 4.76 | 8.44 |
| $[Ag_2(pda)(PPh_3)_4]$ (**25**) | 66.3 | 4.77 | 8.88 | 66.96 | 4.75 | 8.88 |
| $[Ag(hxdaH)(PPh_3)_4].3H_2O$ (**26**) | 65.88 | 5.53 | 8.49 | 65.22 | 4.98 | 8.39 |
| $[Ag_2(hpda)(PPh_3)_4].C_7H_8$ (**27**) | 68.17 | 5.19 | 8.18 | 68.72 | 5.20 | 8.14 |
| $[Ag(odaH)(PPh_3)_2].C_7H_8$ (**28**) | 68.23 | 5.73 | 6.90 | 69.96 | 5.43 | 7.86 |
| $[Ag(ndaH)(PPh_3)_2]$ (**29**) | 65.94 | 5.53 | 7.56 | 65.59 | 4.92 | 8.71 |
| $[Ag_2(dda)(PPh_3)_4].H_2O$ (**30**) | 66.41 | 5.3 | 8.35 | 66.05 | 5.66 | 8.47 |
| $[Ag_2$ (udda) $(PPh_3)_3]$ (**31**) | 64.16 | 5.22 | 7.64 | 64.52 | 5.03 | 7.69 |
| $[Ag_2(udda)(PPh_3)_4]$ (**31A**) | 67.75 | 5.61 | 8.21 | 67.08 | 5.92 | 7.96 |
| $[Ag(dddaH)(PPh_3)_2]$ (**32**) | 66.90 | 5.97 | 7.19 | 66.38 | 5.72 | 8.06 |
| $[Ag_2(uddca)(PPh_3)_5]$ (**33**) | 71.53 | 5.56 | 9.15 | 71.33 | 5.55 | 9.10 |

Complexes **23**-**33** formulate in four categories.

(i) $\{Ag_2(O_2C\text{-}(CH_2)_n\text{-}CO_2(PPh_3)_3\}_n$;

(ii) $[Ag(O_2C\text{-}(CH_2)_n\text{-}CO_2H)(PPh_3)_2]$;

(iii) $[Ag_2(O_2C\text{-}(CH_2)_n\text{-}CO_2)(PPh_3)_4]$ and

(iv) $[Ag(O_2C\text{-}CH_2)_n\text{-}CO_2H(PPh_3)_3]$

Complexes **23** and **31** fall into category (i), complex **28**, **29** and **33** fall into category (ii), complexes **24**, **25**, **27**, **30** and **31A** fall into category (iii) and complex **26** and **32** fall into category (iv).

Crystals of **28** suitable for X-ray structural analysis were obtained when the reaction was carried out in toluene and the mother liquor left to stand for several weeks. The structure of **28** is shown in Figures 53 and 54 and selected bond lengths and angles are listed in Table 18 and 19.

H-bonding links the $Ag(odaH)(PPh_3)_2$ units into a zig-zag one dimensional chain along the b direction (O4 ···· O2 2.573(2)Å, under –x, y-½, -z+½).[71] One toluene solvate

molecule is present for each formula unit and is disordered, it was modelled with 50% occupancy each of two overlapping sites.

The structure is similar to that of complexes **18** (Figure 48) and **22** (Figure 51) with the dicarboxylate only singly deprotonated.The deprotonated group is bound to the silver centre in a chelating mode. The metal is overall four coordinate with the two $PPh_3$ groups completing the ligation around the silver ion. Once again the hydrogen bonding links individual molecules to their neighbours through out the crystal lattice.

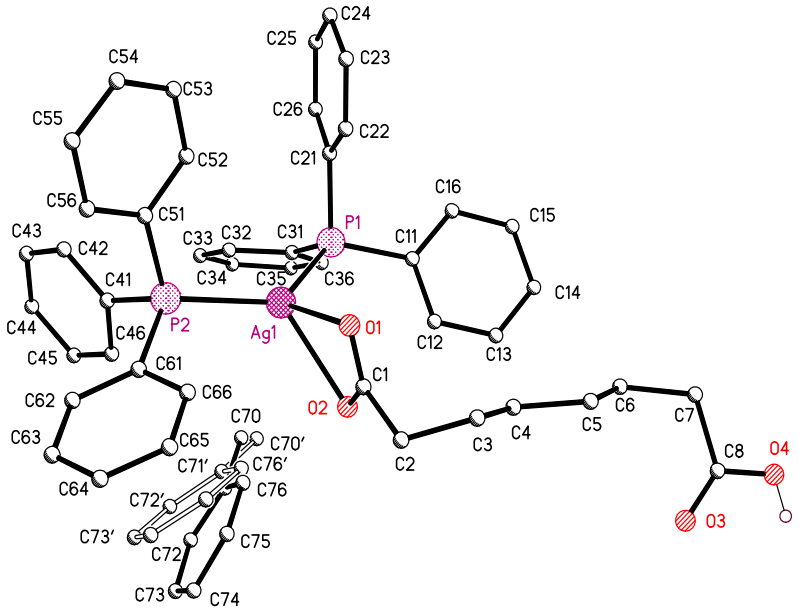



***Figure 53***: Crystal Structure of $[Ag(odaH)(PPh_3)_2].C_7H_8$ (**28**)

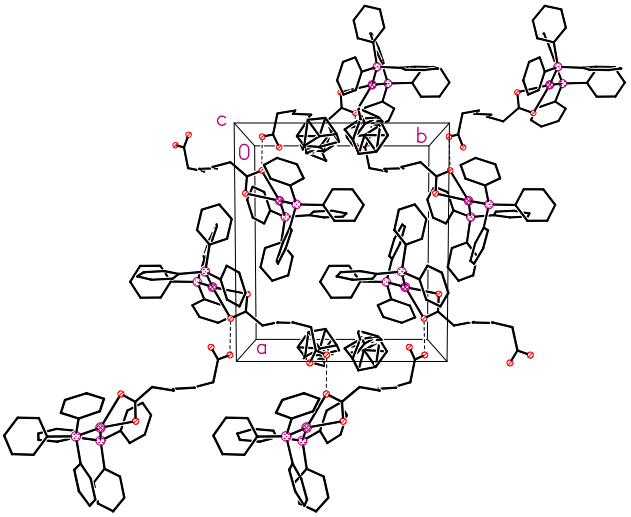



***Figure 54***: Packing diagram for $[Ag(odaH)(PPh_3)_2].C_7H_8$ **(28)**

***Table 18***: Selected bond lengths [Å] and angles [°] around the silver centres in $[Ag(odaH)(PPh_3)_2].C_7H_8$ (**28**)

| | |
|---|---|
| Bond lengths Å | |
| Ag(1)-P(1) | 2.4187(5) |
| Ag(1)-P(2) | 2.4369(5) |
| Ag(1)-O(2) | 2.4690(16) |
| Ag(1)-O(1) | 2.4760(15) |
| Bond angles ° | |
| P(1)-Ag(1)-P(2) | 129.516(19) |
| P(1)-Ag(1)-O(2) | 109.02(5) |
| P(2)-Ag(1)-O(2) | 118.53(5) |
| P(1)-Ag(1)-O(1) | 117.29(4) |
| P(2)-Ag(1)-O(1) | 104.81(4) |
| O(2)-Ag(1)-O(1) | 52.72(5) |

***Table 19***: Hydrogen bonds for {Ag(oda)($PPh_3$)$_2$]$C_7H_9$}n [Å and °]

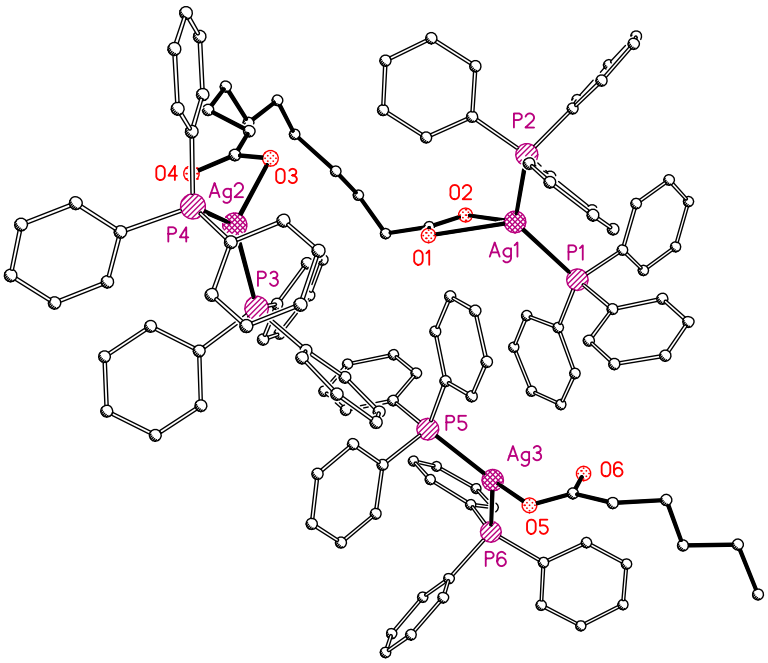
| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(4)-H(4)...O(2)#1 | 0.84 | 1.81 | 2.573(2) | 150.3 |

Symmetry transformations used to generate equivalent atoms: #1 -x,y-1/2,-z+1/2

When the mother liquor from the reaction for complex **31** was allowed to stand, crystals of **31A** were obtained after several weeks. **31A** and **31** do not formulate the same and the x-ray crystal structure of **31A** revealed it to be [$Ag_2$(udda)($pph_3$)$_4$]

The structure of **31A** is shown in Figures 55 and 56 and selected bond lengths and angles are listed in Table 20.

The asymmetric unit contains 1½ independent molecules. The [$Ag_2(PPh_3)_4(O_2C$-R-$CO_2$)] molecule containing Ag1 and Ag2 has no crystallographically imposed symmetry, while that containing Ag3 has a crystallographic 2-fold axis passing through C17 and bisecting the Ag3 ….Ag3A vector.[72] Despite this difference, the structures of the two molecules are similar, in each case two Ag($PPh_3$)$_2$ units are linked by a dicarboxylate chain. The carboxylate binds to Ag1 in a reasonably symmetric manner, but this is not the case for Ag2 or Ag3.




Asymmetric unit – 1½ molecules

***Figure 55***: Crystal Structure [$Ag_2$ (udda) $(PPh_3)_4$]**(31A)**

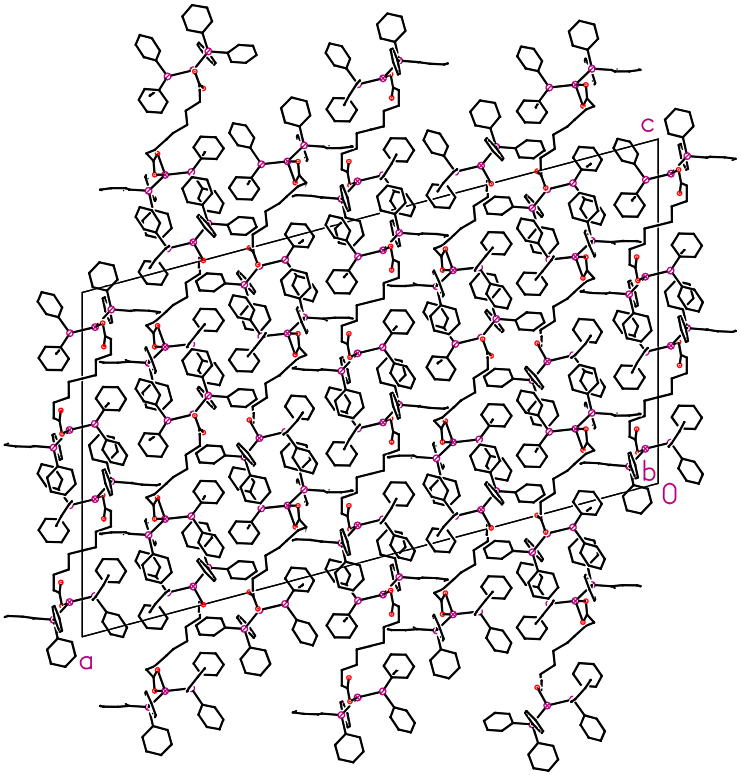



***Figure 56***: Packing diagram for [$Ag_2$ (udda) $(PPh_3)_4$] **(31A)**

Complex **31A** formulates the same as complexes **19** and **20** and it is likely that they all share a similar structure.

***Table 20***: Selected bond lengths [Å] and angles [°] around the silver centres in [$Ag_2$ (udda) $(PPh_3)_4$] **(31A)**

| | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.448(6) |
| Ag(1)-P(2) | 2.4495(18) |
| Ag(1)-P(1) | 2.4535(19) |
| Ag(1)-O(2) | 2.526(6) |
| Ag(2)-O(3) | 2.287(5) |
| Ag(2)-P(4) | 2.4082(19) |
| Ag(2)-P(3) | 2.4425(18) |
| Ag(2)-O(4) | 2.619(6) |
| Ag(3)-O(5) | 2.354(5) |
| Ag(3)-P(6) | 2.4240(18) |
| Ag(3)-P(5) | 2.4547(18) |
| Ag(3)-O(6) | 2.600(5) |
| Bond angles ° | |
| O(1)-Ag(1)-P(2) | 107.51(14) |
| O(1)-Ag(1)-P(1) | 125.12(14) |
| P(2)-Ag(1)-P(1) | 123.99(6) |
| O(1)-Ag(1)-O(2) | 52.06(18) |
| P(2)-Ag(1)-O(2) | 123.83(13) |
| P(1)-Ag(1)-O(2) | 104.36(13) |
| O(3)-Ag(2)-P(4) | 120.79(15) |
| O(3)-Ag(2)-P(3) | 107.35(15) |
| P(4)-Ag(2)-P(3) | 131.28(7) |

| | |
|---|---|
| O(3)-Ag(2)-O(4) | 52.04(18) |
| P(4)-Ag(2)-O(4) | 114.09(16) |
| P(3)-Ag(2)-O(4) | 100.47(17) |
| O(5)-Ag(3)-P(6) | 120.92(13) |
| O(5)-Ag(3)-P(5) | 98.71(13) |
| P(6)-Ag(3)-P(5) | 128.95(7) |
| O(5)-Ag(3)-O(6) | 52.69(17) |
| P(6)-Ag(3)-O(6) | 105.58(13) |
| P(5)-Ag(3)-O(6) | 124.53(13) |

Crystals of **32** suitable for X-ray structural analysis were obtained when the mother liquor was left to stand for several weeks. It should be noted that no powder was obtained from this reaction. The structure of **32** is shown in Figures 57 and 58 and selected bond lengths and angles are listed in Tables 21 and 22.

H-bonding links the units into a one dimensional chain along the a direction (O4 ···· O2 2.502(2)Å, under x+1, y, z).

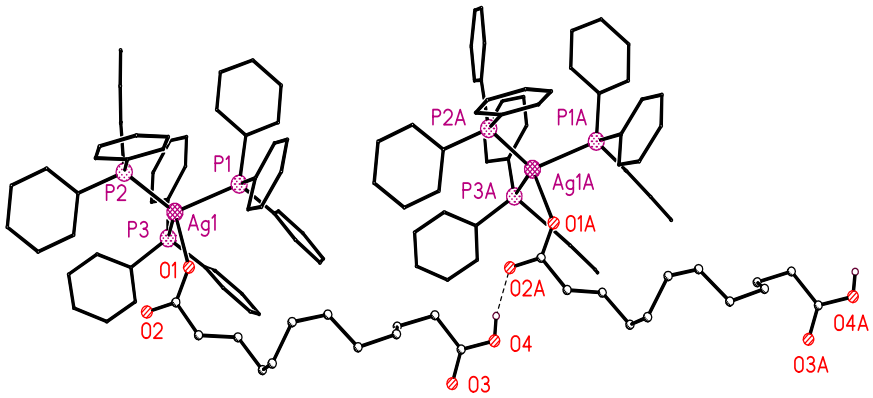



***Figure 57***: Crystal Structure for [Ag(dddaH)($PPh_3$)$_3$] **(32)**

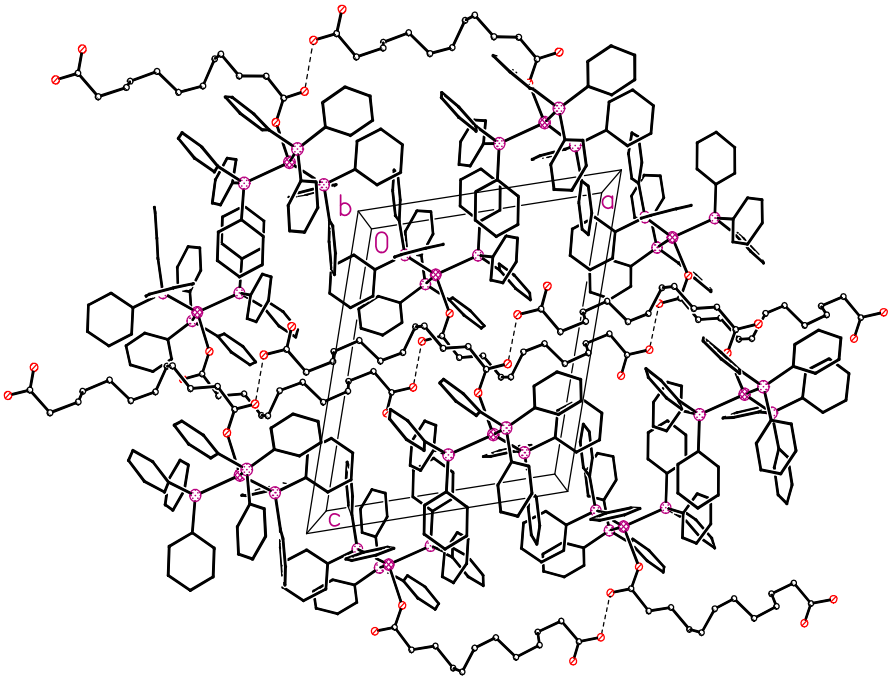



***Figure 58***: Packing diagram for [Ag(dddaH)($PPh_3$)$_3$] (**32**)

The structure of **32** (Figure 58) reveals that the dicarboxylic acid has only singly deprotonated and that the deprotonated carboxylate group is bound to the silver in a monodentate fashion. The silver ion is four coordinate with three $PPh_3$ groups completing the ligation. The tetrahedral silver complexes are hydrogen bonded to neighbours through the hydroxyl hydrogen of the COOH groups in one molecule and the uncoordinated carboxylate oxygen (O2A) of another molecule (Figures 59 and 60)

***Table 21***: Selected bond lengths [Å] and angles [°] around the silver centres in [Ag(dddaH)$(PPh_3)_3$] **(32)**

| Complex (32) | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.3488(13) |
| Ag(1)-P(2) | 2.4792(5) |
| Ag(1)-P(3) | 2.5035(5) |
| Ag(1)-P(1) | 2.5820(5) |
| Bond angles ° | |
| O(1)-Ag(1)-P(2) | 109.29(4) |
| O(1)-Ag(1)-P(3) | 107.63(4) |
| P(2)-Ag(1)-P(3) | 119.209(15) |
| O(1)-Ag(1)-P(1) | 90.20(4) |
| P(2)-Ag(1)-P(1) | 116.060(15) |
| P(3)-Ag(1)-P(1) | 110.240(15) |

***Table 22***: Hydrogen bonds for [Ag(dddaH)$(PPh_3)_3$] **(32)**

[Å and °]

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(4)-H(4)...O(2)#1 | 0.84 | 1.69 | 2.502(2) | 162.6 |

Symmetry transformations used to generate equivalent atoms: #1 x+1,y,z

Crystals of **33** suitable for X-ray structural analysis were obtained when the mother liquor was left to stand for several weeks. Again no powder was obtained from this reaction. The structure of **33** is shown in Figures 59 and 60 and selected bond lengths

and angles are listed in Tables 23 and 24. H-bonds link the $Ag(PPh_3)_2(HOOC(CH_2)_{11}COO)$ units into centrosymmetric dimers (O1-O4A 2.552(2) Å).(Figure 58)

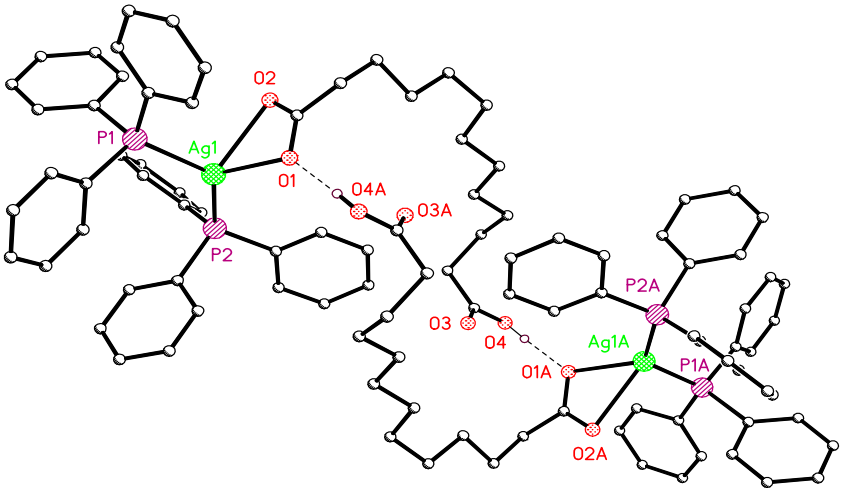



***Figure 59***: Crystal Structure for $[Ag(uddcaH)(PPh_3)_2]$ **(33)**

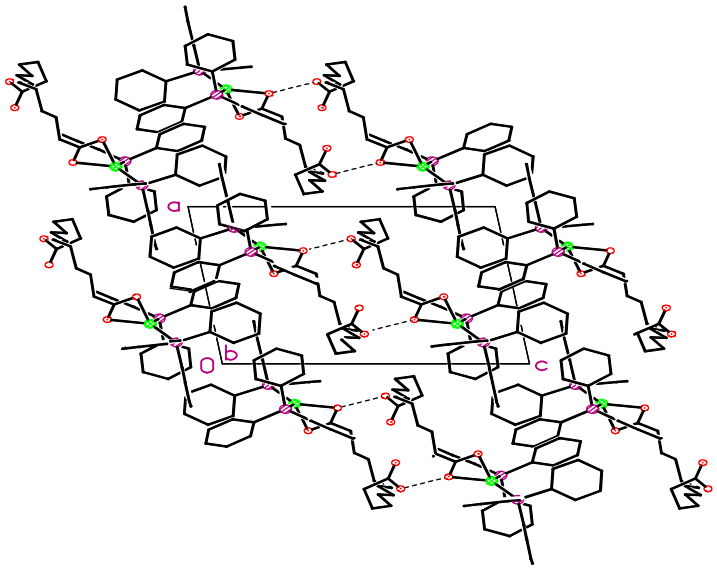



***Figure 60***: Packing diagram for $[Ag(uddcaH)(PPh_3)_2]$ **(33)**

***Table 23***: Selected bond lengths [Å] and angles [°] around the silver centres in [Ag(uddcaH)($PPh_3$)$_2$] **(33)**

| | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1) | 2.3675(17) |
| Ag(1)-P(2) | 2.3966(6) |
| Ag(1)-P(1) | 2.4505(6) |
| Ag(1)-O(2) | 2.5114(18) |
| Bond angles ° | |
| O(1)-Ag(1)-P(2) | 124.63(4) |
| O(1)-Ag(1)-P(1) | 103.79(4) |
| P(2)-Ag(1)-P(1) | 129.51(2) |
| O(1)-Ag(1)-O(2) | 53.38(6) |
| P(2)-Ag(1)-O(2) | 122.21(5) |
| P(1)-Ag(1)-O(2) | 96.60(5) |

***Table 24***: Hydrogen bonds for [Ag(uddcaH)($PPh_3$)$_2$] **(33)**
[Å and °].

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(4)-H(4O)...O(1)#1 | 0.84 | 1.72 | 2.552(2) | 173.6 |

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1

Complex **33** formulates the same as complexes **18** and **22** and has a very similar hydrogen bonded dimeric structure to that of **22** (Figure 50).

The IR spectra of complex **23-33** are shown in the Appendix 1. The IR spectral data that are indicative of structural features of complexes **23-33** are shown in Table 25, 26.The

spectral features of complexes **29** and **33** are similar to those of the structurally characterized **28** and it is likely they share similar structural features based on formulation and IR spectral features.[60] Complexes **24**, **25**, **27** and **30** are probably quite similar to **31A** in structure. Complex **26** formulates as $[Ag(hxdaH)(PPh_3)_3].3H_2O$ and its IR spectrum suggests that it has a similar structure to that of **32**. The presence of a C=O stretch in the IR spectra of complexes **26**, **28**, **29**, **32** and **33** supports the presence of un-dissociated-COOH groups in their formulae.

Complexes **23** and **31** are unusual as they formulate as $[Ag_2(dicarboxylate)(PPh_3)_3]$. The structurally characterized complex **17** has the same formulation and its IR spectrum is similar to those of **23** and **31**. It is possible that **23** and **31** are similar in structure to **17** (Figure 46).

Complexes **23**-**33** were found to have very limited solubility in organic solvents and all attempts to obtain NMR spectra and conductivity readings of the complexes were unsuccessful due to the insolubility of the compounds.

***Table 25***: Characteristic IR bands($cm^{-1}$, KBr discs) of the complexes (**23**)-(**31**) along with the free ligand $PPh_3$

| | $PPh_3$ | (**23**) | (**24**) | (**25**) | (**26**) | (**27**) | **(28)** | **(29)** | **(30)** | **(31)** |
|---|---|---|---|---|---|---|---|---|---|---|
| ν (C-H) aeromatic | | * | 3051 | * | 3057 | 3048 | * | 3053 | 3051 | * |
| ν (C-H) aliphatic | | * | * | * | 2931 | * | 2921,2851 | 2931 | 2921,2850 | * |
| ν (C=O) | | | | | 1708 | | 1704 | 1700 | | * |
| **Carboxylate band** | | | | | | | | | | |
| ν (asym)(OCO) | | 1546 | 1542 | 1548 | 1555 | 1546 | 1547 | 1551 | 1479 | 1557 |
| ν (sym)(OCO) | | 1317 | 1386 | 1391 | 1395 | 1394 | 1399 | 1389 | 1283 | 1384 |
| Δ OCO | | 229 | 156 | 157 | 160 | 152 | 148 | 162 | 196 | 173 |
| **Phosphine bands νC-P** | | | | | | | | | | |
| νasym | 744 | 742 | 743 | 743 | 745 | 747 | 747 | 744 | 752 | 743 |
| νsym | 692 | 694 | 694 | 693 | 694 | 693 | 694 | 694 | 694 | 694 |

* Bands precluded by others in the infrared spectrum.

***Table 26***: Characteristic IR bands ($cm^{-1}$, KBr discs) of the complexes **31-33** along with the free ligand

| | $PPh_3$ | (**31A**) | (**32**) | **(33)** |
|---|---|---|---|---|
| ν (C-H) aeromatic | | 3052 | 3052 | 3054 |
| ν (C-H) aliphatic | | 2921,2853 | 2923 | 2922,2851 |
| ν (C=O) | | 1717 | 1703 | |
| **Carboxylate band** | | | | |
| ν (asym)(OCO) | | 1557 | 1585 | 1574 |
| ν (sym)(OCO) | | 1395 | 1409 | 1401 |
| Δ OCO | | 162 | 176 | 173 |
| **Phosphine bands νC-P** | | | | |
| νasym | 744 | 743 | 744 | 745 |
| νsym | 692 | 694 | 694 | 695 |

## D.4 SYNTHESIS OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$)

Attempts to react complexes **1-11** with $PPh_3$ in a 1:6 ratio yielded the same product as obtained when 4 equivalents of $PPh_3$ were employed and where the dicarboxylate ligands were propanedioate (prda), butanedioate (bda), pentanedioate (pda), nonanedioate (nda) and decanedioate (dda). The synthetic route to the six novel complexes $[Ag(hxdaH)(PPh_3)_3].C_7H_8$ (**34**), $Ag_2(hpda)(PPh_3)_5].C_7H_8$ (**35**) $[Ag_2(oda)(PPh_3)_5].2C_7H_8$ **(36)** $[Ag_2(udda)(PPh_3)_4]$ **(37)**, $[Ag_2(uddca)(PPh_3)_5]$ **(38)**, $[Ag_2(uddca)(PPh_3)_6]$ **(38A)** is shown in Scheme 4.

$[Ag_2(OOC\text{-}(CH_2)_n\text{-}COO)] + 6PPh_3$

Reflux 2.5hrs | Toluene 30ml

$[Ag_x(OOC\text{-}(CH_2)_n\text{-}COOH_y)(PPh_3)_2]$

where n= 4-6 and 9,11; x= 2; y= 0 or 1 and z= 3-6

***Scheme 4***: The synthetic route to silver(I) dicarboxylate complexes with triphenylphosphine.

Compounds **34** to **38** were obtained as white powders and were formulated as shown below in Table 27.

***Table 27***: Elementary Analysis of complexes **34** to **38**

| Complex | Elementary Analysis | | | | | |
|---|---|---|---|---|---|---|
| | % Calculated | | | % Found | | |
| | C | H | P | C | H | P |
| $[Ag(hxdaH)(PPh_3)_2].C_7H_8$ (**34**) | 64.87 | 5.06 | 7.97 | 64.78 | 5.13 | 7.80 |
| $[Ag_2(hpda)(PPh_3)_5].C_7H_8$ (**35**) | 70.28 | 5.27 | 8.71 | 70.64 | 5.17 | 9.67 |
| $[Ag_2(oda)(PPh_3)_4].2C_7H_8$ (**36**) | 69.63 | 5.47 | 7.64 | 69.02 | 5.44 | 7.86 |
| $[Ag_2(udda)(PPh_3)_4]$ (**37**) | 67.40 | 5.32 | 8.38 | 67.28 | 5.27 | 8.51 |
| $[Ag_2(uddca)(PPh_3)_5]$ $C_7H_8$ (**38**) | 70.97 | 5.69 | 8.32 | 70.87 | 5.57 | 9.03 |

When the mother liquor from the reaction for complex **38** was set aside crystals of $[Ag_2(uddca)(PPh_3)_6]$ **38A** deposited after several weeks. These crystals were suitable for x-ray crystallographic analysis. The structure of **38A** is shown in Figures 61 and 62 and selected bond lengths and angles are listed in Table 28.

The structure consists of centrosymmetric dimers linked by a dicarboxylate chain.[73] The chain is disordered and this has been modelled using two overlapping chains of equal occupancy. The disorder is not resolved by refinement in the lower symmetry space group.

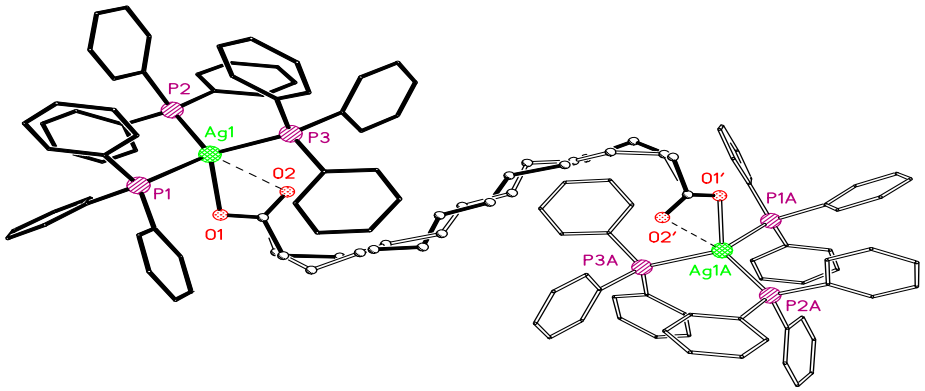



***Figure 61***: Crystal Structure of $[Ag_2(uddca)(PPh_3)_5].C_7H_8$ **38A**

The structure of **38A** is dinuclear with two pseudo-penta coordinated silver ions. The carboxylate groups are almost chelating the metal centres with one definite bonding Ag-oxygen interaction (2.37Å for Ag1-O1) (Table 28).The second oxygen O2 is weakly bound to the silver with a bonding distance of 3.03 Å (Table 23). The geometry around each silver is completed by phosphorous atoms from three $PPh_3$ groups. It is most likely the resultant steric crowding that prevents the carboxylate group from chelating fully to the silver ions as seen for $[Ag_2(udda)(PPh_3)_4]$ **31A** (Figure 55 and Table 20). The molecules of **38A** do not associate by any hydrogen bonding in the crystal (Figure 62)

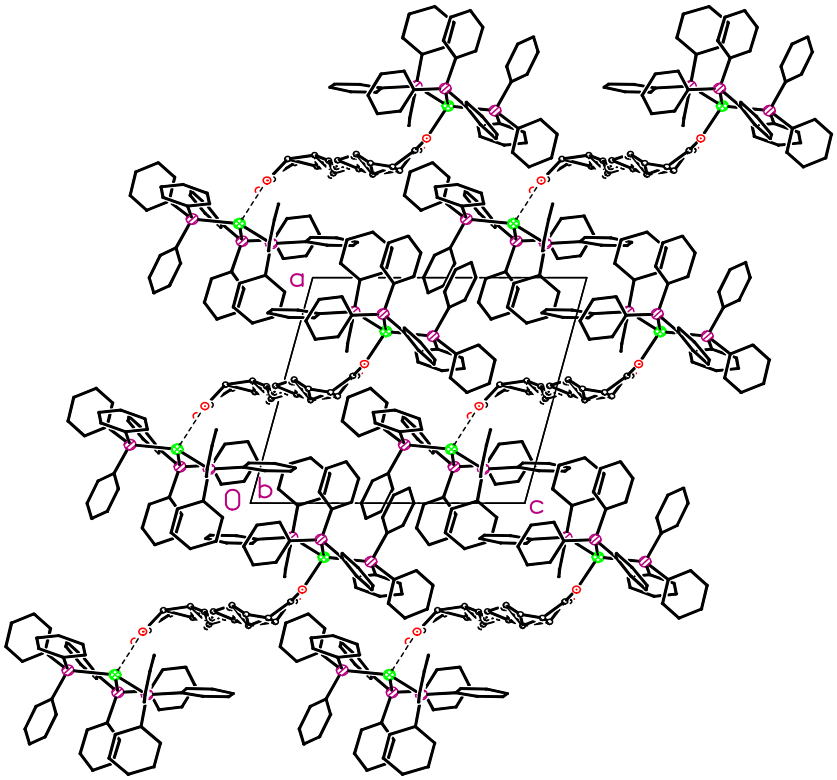



***Figure 62***: Packing diagram for $[Ag_2(uddca)(PPh_3)_6]$ **38A**

***Table 28***: Selected bond lengths [Å] and angles [°] around the silver centres in $[Ag_2(uddca)(PPh_3)_6]$ **38A**

| | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(1')#1 | 2.341(9) |
| Ag(1)-O(1) | 2.370(6) |
| Ag(1)-P(2) | 2.5216(5) |
| Ag(1)-P(3) | 2.5468(5) |
| Ag(1)-P(1) | 2.6753(5) |
| Ag(1)-O(2) | 3.030(5) |
| Bond angles ° | |
| O(1')#1-Ag(1)-O(1) | 2.6(4) |
| O(1')#1-Ag(1)-P(2) | 116.7(3) |
| O(1)-Ag(1)-P(2) | 119.10(14) |
| O(1')#1-Ag(1)-P(3) | 110.1(2) |
| O(1)-Ag(1)-P(3) | 108.95(15) |
| P(2)-Ag(1)-P(3) | 116.569(15) |
| O(1')#1-Ag(1)-P(1) | 83.9(2) |
| O(1)-Ag(1)-P(1) | 82.16(9) |
| P(2)-Ag(1)-P(1) | 112.274(15) |
| P(3)-Ag(1)-P(1) | 113.035(15) |
| O(1')#1-Ag(1)-O(2) | 45.6(3) |
| O(1)-Ag(1)-O(2) | 46.76(12) |
| P(2)-Ag(1)-O(2) | 103.76(9) |
| P(3)-Ag(1)-O(2) | 80.46(11) |
| P(1)-Ag(1)-O(2) | 127.66(9) |

The IR spectra for complexes **34**-**38** are shown in the Appendix 1. The IR spectral data that are indicative of structural features of complexes **34**-**38** are shown in Table 29. The spectra of all five complexes contain $\nu_{asym(OCO)}$ and $\nu_{sym(OCO)}$ bands which are

characteristic of complexes in which carboxylate groups are found bound to a metal centre. The $\Delta_{oco}$ values (148-173 $cm^{-1}$) are in the region expected for chelating or bridging COO groups.[60] Complex 34 formulates as having an undissociated carboxylic acid group with a silver atom and three $PPh_3$ ligands. This is the same formulation as $[Ag(ddaH)(PPh_3)_3]$ (**32**) and the spectral data for **34** suggest that it has a similar structure to **32** (Figure 57).

Complex **37** formulates similarly to complex **31A** and the similarities in the IR spectra support the hypothesis that **37** has a similar structure to that of **31A** (Figure 56). The remaining complexes **35**, **36** and **38** all formulate as $[Ag_2(dicarboxylate)(PPh_3)_5]$. Splitting of the carboxylate bands in the IR spectra of **35**, **36** and **38** supports the presence of two different binding modes for the carboxylate groups in each compound. Complexes **34**-**38** and **38A** were found to have very limited solubility in organic solvents and all attempts to obtain NMR spectra and the conductivity of the complexes were unsuccessful.

***Table 29***: Characteristic IR bands ($cm^{-1}$, KBr discs) of the complexes (**34)**-(**38**) along with the free $PPh_3$ ligand

| | $PPh_3$ | (34) | (35) | (36) | (37) | (38) |
|---|---|---|---|---|---|---|
| ν (C-H) aeromatic | | * | 3045 | 3054 | 3052 | 3052 |
| ν (C-H) aliphatic | | * | 2921 | 2931 | 2923 | 2920 |
| ν (C=O) | | 1723 | | | | |
| **Carboxylate band** | | | | | | |
| ν (asym)(OCO) | | 1547 | 1555 | 1547 | 1556 | 1585 |
| ν (sym)(OCO) | | 1398 | 1382 | 1399 | 1395 | 1434 |
| Δ OCO | | 149 | 173 | 148 | 161 | 151 |
| **Phosphine bands** | | | | | | |
| **νC-P** | | | | | | |
| νasym | 744 | 746 | 743 | 747 | 743 | 744 |
| νsym | 692 | 695 | 693 | 695 | 694 | 694 |

* Bands precluded by others in the infrared spectrum.

## D.5 SYNTHESIS AND CHARACTERISATION OF SILVER(I) DIPHENYLPHOSPHINEMETHANE COMPLEXES

Complexes **1-11** were reacted with bis (diphenylphosphino) methane (dppm) in a 1:2 molar ratio. The synthetic route to the silver dicarboxylate dppm complexes $[Ag_2(prda)(dppm)_3]C_7H_8$ **(39),** $[Ag_2(bda)(dppm)_3].C_7H_8$ (**40**), $[Ag_2(pda)(dppm)_4]$ (**41**), $[Ag_2(hxda)(dppm)_4]$ (**42**), $[Ag_2(hpda)(dppm)_4]$ (**43**), $[Ag_2(oda)(dppm)_4]$ **(44)**, $[Ag_2(nda)(dppm)_4]$ **(45),** $[Ag(ddaH)(dppm)_3].3H_2O$ **(46),** $[Ag_2(udda)(dppm)_4]$ **(47)**, $[Ag_2(ddda)(dppm)_4].H_2O$ **(48)**, $[Ag_2(uddca)(dppm)_4].2H_2O$ **(49)**, $[Ag_2(dppm)_2(OAc)_2].3C_7H_8$ **(49A)** is shown in Scheme 5

$[Ag_2(OOC\text{-}(CH_2)_n\text{-}COO)]$ +2dppm

Reflux
2.5hrs

Tolune
30ml

$\{Ag_x(OOC\text{-}(CH_2)_n\text{-}COOH_y)(dppm)_z\}$

where n=1-11, x=1or 2, y= 0 or 1 and z=3 or 4

***Scheme 5***: The synthetic route to the silver dicarboxylate dppm complexes

Complexes **39** to **49** were obtained as off white powders.The mother liquor from the reaction of complex **48** yielded colourless crystals of $\{Ag_2(OOC\text{-}(CH_2)_{10}COO)(dppm)_2\}_n.H_2O\}$**48A**. Complexes **39-49** were formulated as below in Table 30

***Table 30***: Elementary Analysis of complexes **39** to **49**

| Complex | Elementary Analysis | | | | | |
|---|---|---|---|---|---|---|
| | % Calculated | | | % Found | | |
| | C | H | P | C | H | P |
| $[Ag_2(prda)(dppm)_3].C_7H_8$ (**39**) | 58.24 | 4.89 | 9.19 | 58.72 | 4.50 | 9.98 |
| $[Ag_2(bda)(dppm)_3]. C_7H_8$ (**40**) | 58.61 | 5.02 | 9.07 | 57.40 | 4.31 | 9.97 |
| $[Ag_2(pda)(dppm)_4]$ (**41**) | 59.05 | 4.87 | 11.08 | 58.07 | 4.47 | 10.41 |
| $[Ag_2(hxda)(dppm)_4]$ (**42**) | 60.02 | 5.21 | 10.87 | 59.00 | 4.66 | 10.26 |
| $Ag_2(hpda)(dppm)_4]$ (**43**) | 60.32 | 5.32 | 10.55 | 59.46 | 4.65 | 11.02 |
| $[Ag_2(oda)(dppm)_4]$ (**44**) | 60.62 | 5.43 | 10.42 | 60.47 | 4.99 | 10.00 |
| $[Ag_2(nda)(dppm)_4]$ (**45**) | 60.91 | 5.53 | 10.30 | 59.67 | 4.93 | 10.82 |
| $[Ag(ddaH)(dppm)_3]$ .$3H_2O$ (**46**) | 61.06 | 6.48 | 9.64 | 60.61 | 5.29 | 9.88 |
| $[Ag_2(udda)(dppm)_4]$ (**47**) | 61.48 | 5.73 | 10.07 | 60.84 | 5.15 | 10.46 |
| $[Ag_2(ddda)(dppm)_4].H_2O$ (**48**) | 61.57 | 6.32 | 9.48 | 61.43 | 5.61 | 9.36 |
| $[Ag_2(uddca)(dppm)_4].2H_2O$ (**49**) | 60.29 | 6.07 | 9.57 | 59.71 | 5.25 | 9.93 |

The crystals of **48A** were suitable for X-ray crystallographic analysis.

The structure of **48A** is shown in Figures 63 and 64 and selected bond lengths and angles are listed in Tables 31 and 32.

The structure is a linear polymer in which centrosymmetric $Ag_2(dppm)_2$ units are linked by diacid anions.[74] The chains are linked via H-bonding through the water solvate molecule (one of the hydrogen atoms on the water is necessarily disordered).

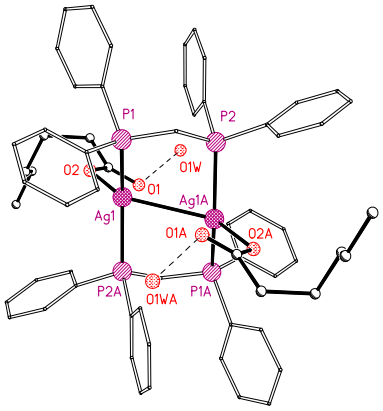



***Figure 63***: Crystal Structure for $\{Ag_2(dppm)_2(ddda)(H_2O)\}_n$ **48A**

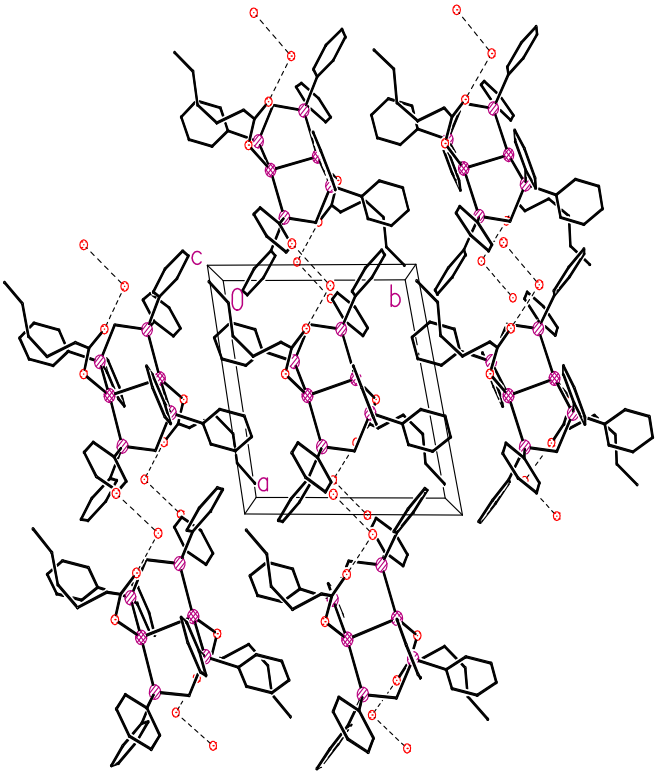



***Figure 64***: Packing diagram for $\{Ag_2(dppm)_2(ddda)(H_2O)\}_n$ **48A**

***Table 31***: Selected bond lengths [Å] and angles [°] around the silver centres in $\{Ag_2(dppm)_2(ddda)(H_2O)\}_n$ **48A**

| Complex (48A) | |
|---|---|
| Bond lengths Å | |
| Ag(1)-O(2) | 2.303(3) |
| Ag(1)-P(1) | 2.4235(9) |
| Ag(1)-P(2)#1 | 2.4295(10) |
| Ag(1)-Ag(1)#1 | 3.0430(7) |
| Bond angles ° | |
| O(2)-Ag(1)-P(1) | 106.66(8) |
| O(2)-Ag(1)-P(2)#1 | 98.96(9) |
| P(1)-Ag(1)-P(2)#1 | 150.47(4) |
| O(2)-Ag(1)-Ag(1)#1 | 132.06(9) |
| P(1)-Ag(1)-Ag(1)#1 | 92.80(2) |
| P(2)#1-Ag(1)-Ag(1)#1 | 80.36(3) |

***Table 32***: Hydrogen bonds for $\{Ag_2(dppm)_2(ddda)(H_2O)\}_n$ **48A** [Å and °]

| D-H...A | d(D-H) | d(H...A) | d(D...A) | <(DHA) |
|---|---|---|---|---|
| O(1W)-H(1WA)...O(1) | 0.86 | 1.92 | 2.782(6) | 179.2 |
| O(1W)-H(1WB)...O(1W)#3 | 0.85 | 1.96 | 2.815(11) | 179.4 |

Symmetry transformations used to generate equivalent atoms: #1 -x+1,-y+1,-z+1 #2 -x,-y,-z+2 #3 -x,-y+1,-z+2

Crystals of $[Ag_2(dppm)_2(OAc)_2].3C_7H_8$, suitable for X-ray structural analysis were obtained when impure complex **10** was reacted with dppm and the reaction was carried out in toluene and the mother liquor left to stand for several weeks. The structure of

$[Ag_2(dppm)_2(OAc)_2].3C_7H_8$, is shown in Figures 65 and 66 and selected bond lengths and angles are listed in Table 33.

The dimeric silver molecule lies on a centre of symmetry, so that the asymmetric unit contains half of the molecule. The asymmetric unit also contains 1.5 toluene molecules; one is disordered about a centre of symmetry and the second is disordered over two overlapping positions. The geometry of the phenyl rings of the latter toluene was restrained to that of a regular hexagon. The acetate bonding is asymmetric but probably best thought of as bidentate.[75] There are some π–π and edge-to-face interactions but that is not unusual for these types of molecules.

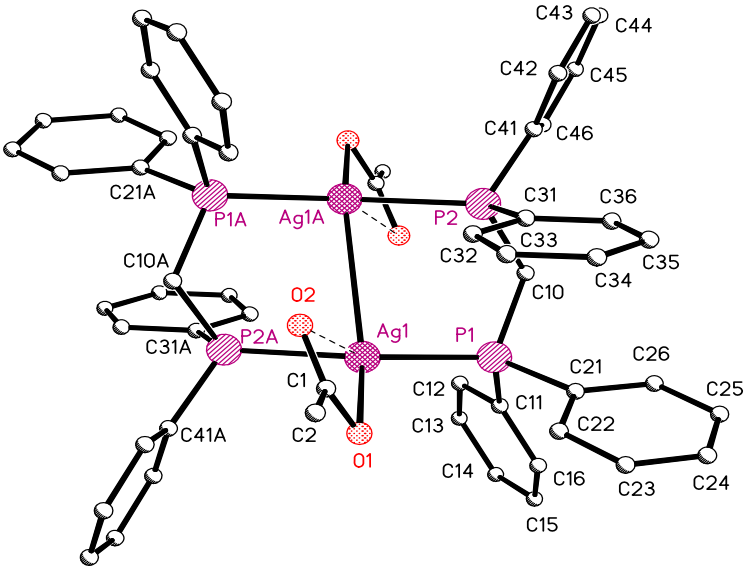



***Figure 65***: Crystal Structure for $[Ag_2(dppm)_2(OAc)_2].3\ C_7H_8$ **49A**

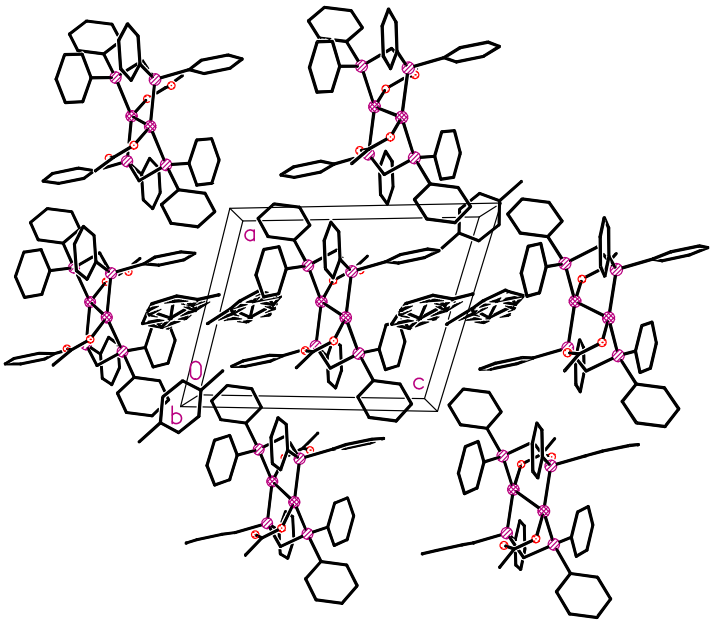



***Figure 66***: Packing diagram for $[Ag_2(dppm)_2(OAc)_2].3C_7H_8$ **49A**

***Table 33***: Selected bond lengths [Å] and angles [°] around the silver centres in $[Ag_2(dppm)_2(OAc)_2].3C_7H_8$

| Complex(54A) | |
|---|---|
| Bond lengths Å | |
| Ag(1)-P(1) | 2.4232(5) |
| Ag(1)-O(1) | 2.4376(14) |
| Ag(1)-Ag(1)#1 | 3.2509(3) |
| Ag(1)-P(2)#1 | 2.4504(4) |
| Ag(1)-O(2) | 2.7053(17) |
| Bond angles ° | |
| P(1)-Ag(1)-O(1) | 107.40(3) |
| P(1)-Ag(1)-P(2)#1 | 146.021(15) |
| O(1)-Ag(1)-P(2)#1 | 102.25(4) |
| P(1)-Ag(1)-O(2) | 130.70(3) |
| O(1)-Ag(1)-O(2) | 50.46(5) |
| P(2)#1-Ag(1)-O(2) | 81.50(3) |
| P(1)-Ag(1)-Ag(1)#1 | 89.779(11) |
| O(1)-Ag(1)-Ag(1)#1 | 140.14(4) |
| P(2)#1-Ag(1)-Ag(1)#1 | 77.551(11) |
| O(2)-Ag(1)-Ag(1)#1 | 90.95(3) |

The formulations for complexes **39**-**49** are such that it is not likely that they share the same structure as that of **48A**. Indeed complxes **39**-**49** formulate in three categories (i) $[Ag_2(O_2C\text{-}CH_2)_n\text{-}CO_2)(dppm)_3]$, (ii) $[Ag_2(O_2C\text{-}(CH_2)_n\text{-}CO_2)(dppm)_4]$ and (iii) $[Ag(O_2C\text{-}CH_2)_n\text{-}CO_2H)(dppm)_3]$ . The complexes **39** and **40** formulate as shown in category (i), complexes **41**-**45** and **47**-**49** formulate as shown in category (ii) and complex **46** is unusual as it formulates as shown in category (iii).

The IR spectra of complexes **39**-**49** (with that of **48A**) are shown in Appendix1. The IR spectral data that are indicative of the structural features of the complexes are shown in Tables 34 and 35. Although the complexes **39** and **40** formulate somewhat similarly they do not appear to have similar structures as evidenced by their IR spectra. In the spectrum of **39** the $\nu_{asym}$ OCO band is split indicating that two carboxylate ligands are bound to the metal centres in different modes.[60] In the IR spectrum of **40** the $\nu_{asym}$ OCO is not split (Table 34). Furthermore, the elemental analytical results for **40** are slightly inconclusive. The spectral bands indicative of the presence of the dppm group (750-680 $cm^{-1}$) are split in the spectra of both **39** and **40** and the shape and position of the bands is different for each complex suggesting that the dppm ligands may be bound to the metal centre in different co-ordination modes for each complex.

The IR spectra for complexes **41**-**45** and **47**-**49** are all very similar. The carboxylate $\nu_{asym}$ OCO and $\nu_{sym}$ OCO bands are not split. The spectra of these complexes also contain bands that are indicative of the presence of the dppm ligands and again the shape and values for these bands suggests that they are bound to the silver centres in similar modes for all eight complexes. A structure that fits the physico-chemical data of complexes **41**-**45** and **47**-**49** is shown in Figure 67. This structural motif is known for silver dppe complexes where the counter ion is $NO^{-3}$.

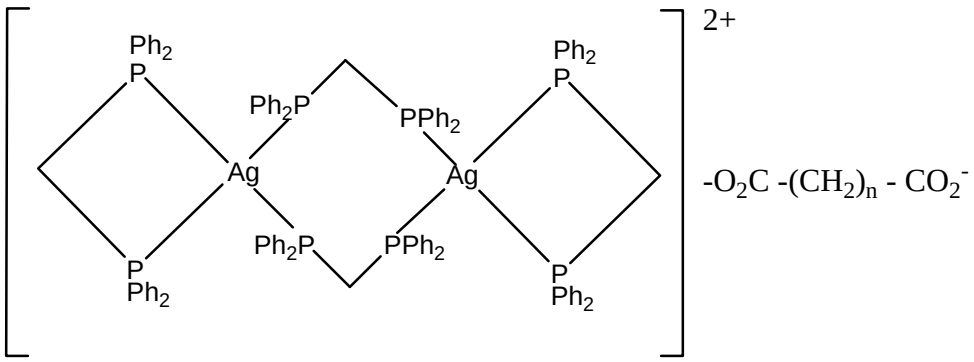



***Figure 67***: Possible structure for complexes **41**-**45** and **47**-**49.**

Complex **46** is unusual in that it appears to have a dicarboxylate group which is only mono- deprotonated. The IR spectrum clearly shows the presence of the C=O band at 1714 $cm^{-1}$ (Table 34) and it formulates as [Ag (ddaH)$(dppm)_3$].3$H_2O$ (although the % hydrogen is low and therefore this formulation may be erroneous like complexes **49** and **40** it is difficult to assign a structure to complex **46**.

Complex **39**-**49** (and complex **48A**) were found to have very limited solubility in organic solvents and all attempts to obtain NMR spectra and the conductivity of complexes were unsuccessful.

***Table 34***: Characteristic IR bands($cm^{-1}$, KBr discs) of the complexes **39-49** along with the free ligand

| | $PPh_3$ | **(39)** | **(40)** | **(41)** | **(42)** | **(43)** | **(44)** | **(45)** | **(46)** | **(47)** | **(48)** | **(49)** |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ν (C-H) aeromatic | | 3049 | 3052 | 3050 | 3049 | 3050 | 3050 | 3051 | 3051 | 3050 | 3052 | 3051,3019 |
| ν (C-H) aliphatic | | * | * | * | 2922 | 2937 | 2940 | 2930 | 2924 | 2922 | 2923 | 2920 |
| | | | | | | | | | 2850 | 2850 | 2850 | 2850 |
| ν (C=O) | | * | * | * | * | * | * | * | 1714 | * | * | * |
| **Carboxylate band** | | | | | | | | | | | | |
| ν (asym)(OCO) | | 1537 | 1547 | 1557 | 1555 | 1559 | 1561 | 1553 | 1555 | 1552 | 1563 | 1560 |
| ν (sym)(OCO) | | 1434 | 1385 | 1382 | 1390 | 1395 | 1390 | 1392 | 1387 | 1395 | 1386 | 1397 |
| Δ OCO | | 103 | 162 | 175 | 165 | 164 | 171 | 161 | 168 | 157 | 177 | 163 |
| **Phosphine bands** | | | | | | | | | | | | |
| **νC-P** | | | | | | | | | | | | |
| νasym | 744 | 737 | 736 | 737 | 739 | 738 | 740 | 741 | 740 | 740 | 740 | 740 |
| νsym | 692 | 692 | 693 | 696 | 695 | 694 | 694 | 694 | 695 | 693 | 695 | 694 |

* Bands precluded by others in the infrared spectrum.

***Table 35***: Characteristic IR bands ($cm^{-1}$, KBr discs) of the complexes (54A**)** along with the free ligand

| | **$PPh_3$** | **(48A)** |
|---|---|---|
| ν (C-H) aeromatic | | 3052 |
| ν (C-H) aliphatic | | 2920 |
| ν (C=O) | | 1717 |
| **Carboxylate band** | | |
| ν (asym)(OCO) | | 1585 |
| ν (sym)(OCO) | | 1401 |
| Δ OCO | | 184 |
| **Phosphine bands** | | |
| **νC-P** | | |
| νasym | 744 | 744 |
| νsym | 692 | 694 |

## D.6 SYNTHESIS OF SILVERDICARBOXYLATE DIPHENYLPHOSPHINE ETHANE COMPLEXES

Complexes **1-11** were reacted with bis(diphenylphosphino)ethane(dppe) in a 1:2 molar ratio using the same procedure employed for the dppm reactions to yield the complexes $[Ag_2(prda)(dppe)_4].H_2O$ (**50**), $[Ag_2(bda)(dppe)_4]$(**51**), $[Ag_2(pda)(dppe)_3].4H_2O$(**52**), $[Ag_2(hxda)(dppe)_4]$ (**53**), $[Ag_2(hpda)(dppe)_3]$ (**54**), $[Ag_2(oda)(dppe)_4]$(**55**), $[Ag_2(nda)(dppe)_4].2H_2O$ (**56**), $[Ag_2(dda)(dppe)_4]$ (**57**), $[Ag_2(udda)(dppe)_4].H2O$ (**58**), $[Ag_2(ddda)(dppe)_4]$ (**59**), $[Ag_2(uddca)(dppe)_4]$(**60**)

Complexes **50**-**60** were obtained as off white powders and they were formulated as shown in Table 36.

***Table 36***: Elementary Analysis of complexes **50** to **60**

| Complex | Elementary Analysis | | | | | |
|---|---|---|---|---|---|---|
| | % Calculated | | | % Found | | |
| | C | H | P | C | H | P |
| **$[Ag_2(prda)(dppe)_4].H_2O$ (50)** | 59.41 | 5.41 | 10.39 | 58.24 | 4.48 | 11.32 |
| **$[Ag_2(bda)(dppe)_4]$ (51)** | 60.62 | 5.43 | 10.42 | 59.63 | 4.75 | 10.98 |
| **$[Ag_2(pda)(dppe)_3].4H2O$ (52)** | 53.22 | 5.61 | 8.76 | 52.17 | 4.21 | 9.46 |
| **$[Ag_2(hxda)(dppe)_4]$ (53)** | 61.20 | 5.63 | 10.18 | 61.78 | 5.10 | 10.53 |
| **$[Ag_2(hpda)(dppe)_3]$ (54)** | 57.89 | 5.45 | 9.14 | 56.84 | 4.80 | 10.26 |
| **$[Ag_2(oda)(dppe)_4]$ (55)** | 61.75 | 5.83 | 9.95 | 60.13 | 5.02 | 10.25 |
| **$[Ag_2(nda)(dppe)_4].2H_2O$ (56)** | 60.29 | 6.07 | 9.57 | 60.43 | 5.17 | 10.71 |
| **$[Ag_2(dda)(dppe)_4]$ (57)** | 62.27 | 6.02 | 9.73 | 62.52 | 5.57 | 10.29 |
| **$[Ag_2(udda)(dppe)_4].H_2O$ (58)** | 61.67 | 6.18 | 9.49 | 61.49 | 5.51 | 9.29 |
| **$[Ag_2(ddda)(dppe)_4]$ (59)** | 62.78 | 6.20 | 9.52 | 63.62 | 5.74 | 9.59 |
| **$[Ag_2(uddca)(dppe)_4]$ (60)** | 63.02 | 6.29 | 9.42 | 62.40 | 5.66 | 9.89 |

Complexes **50**-**60** formulate into two categories (i) $[Ag_2(O_2C\text{-}(CH_2)_n\text{-}CO_2)(dppe)_3]$ and (ii) $[Ag_2(O_2C(CH_2)_n\text{-}CO_2)(dppe)_4]$. Complexes **52** and **55** formulate in category (i) whilst the remaining nine complexes formulate in category (ii).

The IR spectra of complexes **50**-**60** are shown in the Appendix 1 and the IR spectral bands indicative of structural features are listed in Table 37. The spectra are all very

similar with the carboxylate bands ($\nu_{asym}$ OCO and $\nu_{sym}$ OCO) for all complexes being unsplit. Furthermore, all of the IR spectra of the complexes contain bands that are characteristic of the presence of the dppe ligands (790-680 $cm^{-1}$). It is most likely that complexes **50**, **51**, **53** and **55-60** have structures similar to their dppm counterparts (complexes **41-45** and **47-49**) and that of the published nitrate silver dppe complex salt (Figure 68).

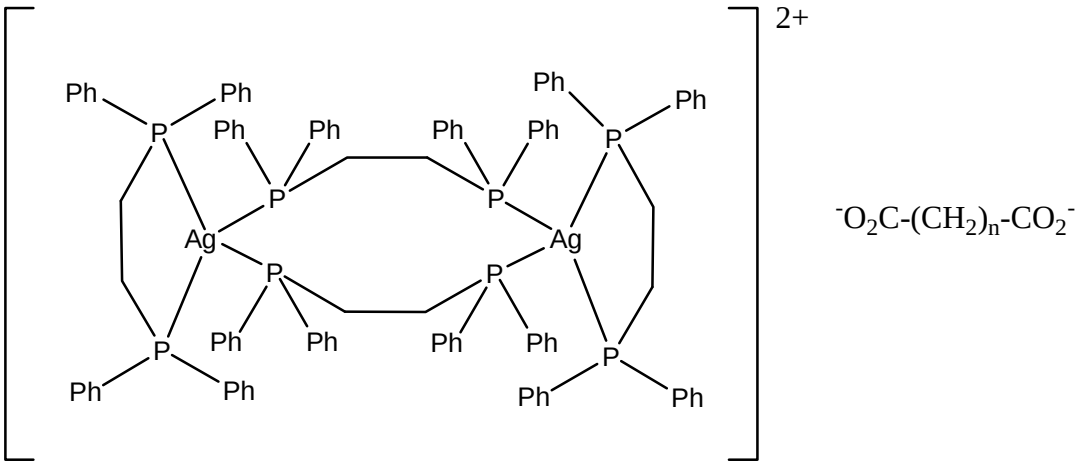



***Figure 68***: Possible structure for complexes **50**, **51**, **53**, and **55-60**

Complexes **50-60** were found to have very limited solubility in organic solvents and all attempts to obtain NMR spectra and the conductivity of the complexes were unsuccessful due to the insolubility of the compounds.

***Table 37***: Characteristic IR bands($cm^{-1}$, KBr discs) of the complexes **50-60** along with the free ligand

| | $PPh_3$ | (**50**) | (**51**) | (**52**) | (**53**) | (**54**) | (**55**) | (**56**) | (**57**) | (**58**) | (**59**) | (**60**) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| ν (C-H) aeromatic | | 3052 | 3052 | 3050 | 3049 | 3049 | * | 3050 | 3052 | 3052 | 3052 | 3052 |
| ν (C-H) aliphatic | | * | 2915 | * | 2919 | 2927 | 2935 | 2923 | 2924 | 2923 | 2920 | 2923 |
| | | | | | | | | | 2851 | 2850 | 2849 | 2850 |
| ν (C=O) | | * | * | * | * | * | * | * | * | * | * | * |
| **Carboxylate band** | | | | | | | | | | | | |
| ν (asym)(OCO) | | 1556 | 1552 | 1552 | 1555 | 1548 | 1545 | 1561 | 1556 | 1550 | 1555 | 1551 |
| ν (sym)(OCO) | | 1434 | 1405 | 1400 | 1403 | 1401 | 1398 | 1399 | 1404 | 1399 | 1403 | 1400 |
| Δ OCO | | 122 | 147 | 152 | 152 | 147 | 147 | 162 | 152 | 151 | 152 | 151 |
| **Phosphine bands** | | | | | | | | | | | | |
| **νC-P** | | | | | | | | | | | | |
| νasym | 744 | 742 | 744 | 741 | 741 | 743 | 740 | 742 | 745 | * | 743 | 743 |
| νsym | 692 | 694 | 694 | 694 | 692 | 693 | 693 | 695 | 695 | 695 | 695 | 695 |

* Bands precluded by others in the infrared spectrum

## D.7 ANTIMICROBIAL ACTIVITY OF THE SILVER (I) DICARBOXYLATE

The onset of antibacterial resistance to these therapeutic treatments exerted considerable pressure on scientists and clinicians to develop novel, targeted multi-modal antibacterial agents with minimal cytotoxicity to mammalian cells.

The decline in the number of available antibacterial therapies for the treatment of multi-drug resistant pathogens, has resulted in a reversion to older antimicrobial metallic agents, such as silver. In clinical terms, silver is the antimicrobial metal best known for its broad spectrum activity against intractable infectious microorganisms, including antibiotic resistant strains.[76] The multiple modes of action of the silver ion include binding with cell DNA, inhibiting enzymes that mediate respiration and reacting with sensitive thiol groups on bacterial proteins - thereby destroying the normal biological activity of the protein. A key advantage of employing silver based inorganic antimicrobials instead of traditional silver nitrate is the potential for controlled release of silver ions and reduced photosensitivity. The success of these silver based antimicrobials depends on the appropriate ancillary ligands and the stabilization of specific oxidation states. In addition, they play a pivotal role in modifying reactivity and lipophilicity. It has been reported that the primary challenge in designing silver based antimicrobial drugs lies in the slow and sustained release of $Ag^{+}$ ions over a period of time.[77] However if the ligands are too tightly bound to the metal centre, this can impede the release of the silver ions. This can result in compromised and reduced antibacterial activity with the potential for silver resistant microorganisms.

### D.7.1 Antifungal agents in clinical use

There are four major classes of systemic antifungal compounds currently in clinical use: the polyene antibiotics, the azole derivatives, the allyamines and thiocarbamates, and the morpholines.[78] The first three are targeted against ergosterol, the major fungal sterol in the plasma membrane. Echinocandins (a recent discovery) are successors to cilofungin, which was abandoned in the 1980s. The echinocandins inhibit synthesis of fungal β-1,3 glucan, and this represents the first novel target in 20 years of antifungal drug discovery in terms of clinically useful drugs. Of these the polyene antibiotics and the azole derivatives are the most effective.

All of the novel silver complexes **1-60** generated during this project were assessed for anti-microbial activity against fungal (*Candida albicans*) and bacterial (Grampositive and Gramnegative) cells over a range of concentrations.

### D.7.2 Antifungal activity of the complexes

The complexes were assessed for their ability to inhibit growth of an isolate of *C.albicans* over a range of concentrations in minimal media (Tables 38-41). The antifungal activity of these complexes was compared to that of (i) Silver Nitrate (Ag $NO_3$) and Silver acetate [$Ag(CH_3COO)$] {known sources of simple $Ag^+$ ions}(Table 38) (ii) Amphotericin B (Amp B) a well known antifungal drug (Table 41**)** and (iii) the metal free dicarboxylic acid, $PPh_3$, dppm and dppe ligands (Table 41**).** Tables 38-41 also list the $IC_{50}$ values for each of the compounds.

The experiments were carried out as described in the experimental section, each sample was tested in tripclicate and each experiment was repeated three times. The results shown represent the average of these results. The percentage growth of strain of *C.albicans* ATCC 10231on $AgNO_3$ was 79% at 0.08 µg/ml and 18% at 1µg/ml with an $IC_{50}$ (concentration that causes 50% reduction in cell viability) of 0.1µg/ml. For silver acetate the sensitivity is similar with 80% at 0.08 µg/ml and 20% at 1µg/ml with $IC_{50}$ 0f 0.1µg/ml. For Amphotericin B the percentage growth was 6% at 1.0 µg/ml.

***Table 38***: Anti-*Candida* activity and $IC_{50}$ values of silver dicarboxylate complexes **1-11** and $AgNO_3$ & $[AgCH_3COO]$

| **Compound** | **% growth at concentration (µg/ml)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **1.0** | **0.5** | **0.1** | **0.09** | **0.08** | **$IC_{50}$ (µg /ml)** | **$IC_{50}$ (µM)** |
| **$[Ag_2(prda)]$(1)** | 23 | 54 | 70 | 81 | 89 | 0.5 | 1.57 |
| **$[Ag_2(bda)]$(2)** | 16 | 28 | 35 | 50 | 77 | 0.09 | 0.27 |
| **$[Ag_2(pda)]$(3)** | 22 | 35 | 41 | 59 | 69 | 0.09 | 0.26 |
| **$[Ag_2(hxda)]$(4)** | 07 | 16 | 25 | 36 | 52 | 0.08 | 0.22 |
| **$[Ag_2(hpda)]$(5)** | 11 | 45 | 55 | 65 | 89 | 0.1 | 0.26 |
| **$[Ag_2(oda)]$(6)** | 09 | 16 | 34 | 47 | 50 | 0.08 | 0.20 |
| **$[Ag_2(nda)]$(7)** | 12 | 36 | 51 | 65 | 78 | 0.1 | 0.24 |
| **$[Ag_2(dda)]$(8)** | 05 | 25 | 35 | 46 | 80 | 0.09 | 0.21 |
| **$[Ag_2(udda)]$(9)** | 06 | 52 | 58 | 75 | 89 | 0.5 | 1.16 |
| **$[Ag_2(ddda)]$(10)** | 17 | 29 | 38 | 50 | 76 | 0.09 | 0.20 |
| **$[Ag_2(uddca)]$(11)** | 15 | 34 | 48 | 68 | 82 | 0.1 | 0.21 |
| **$Ag\ NO_3$** | 18 | 25 | 45 | 60 | 79 | 0.1 | 0.58 |
| **$[Ag(CH_3COO)]$** | 20 | 38 | 52 | 65 | 80 | 0.1 | 0.59 |

***Table 39***: Anti-*Candida* activity and $IC_{50}$ values of $PPh_3$ complexes **12-38**

| **Compound** | **% growth at concentration (µg /ml)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **20** | **10** | **5** | **2.5** | **1.0** | **$IC_{50}$ (µg /ml)** | **$IC_{50}$ (µM)** |
| **$[Ag_2(prdaH)(PPh_3)_2].C_7H_8$ (12)** | 16 | 45 | 53 | 94 | - | 5 | 5.3 |
| **$[Ag_2(bda)(PPh_3)_3].C_7H_8$ (13)** | 18 | 45 | 56 | 92 | - | 5 | 4.1 |
| **$[Ag_2(pda)(PPh_3)_3].2H_2O$ (14)** | 15 | 28 | 50 | 59 | 65 | 5 | 4.2 |
| **$[Ag_2(hxda)(PPh_3)_2]$ (15)** | 19 | 25 | 38 | 50 | 75 | 2.5 | 2.8 |
| **$[Ag_2(hpda)(PPh_3)_2].2H_2O$ (16)** | 15 | 29 | 37 | 48 | 86 | 2.5 | 2.6 |
| **$\{[Ag_2(oda)(PPh_3)_3].2H_2O\}_n$(17)** | 13 | 26 | 40 | 52 | 68 | 2.5 | 2.1 |
| **$[Ag(ndaH)PPh_3)_2]$ (18)** | 18 | 34 | 46 | 50 | 75 | 2.5 | 3.1 |
| **$[Ag_2(dda)(PPh_3)_4].2C_7H_8$ (19)** | 06 | 26 | 38 | 45 | 85 | 2.5 | 1.5 |
| **$[Ag_2(udda)(PPh_3)_2]$ (20)** | 12 | 34 | 52 | 68 | 76 | 5 | 5.2 |
| **$[Ag_2(ddda)(PPh_3)_3]$(21)** | 09 | 26 | 37 | 52 | 65 | 2.5 | 2.0 |
| **$[Ag(uddcaH)(PPh_3)_2]$ (22)** | 12 | 24 | 39 | 50 | 68 | 2.5 | 2.8 |
| **$[Ag_2(prda)(PPh_3)_3].H_2O$ (23)** | 25 | 45 | 56 | 86 | - | 5 | 4.4 |
| **$[Ag_2(bda)(PPh_3)_4]$ (24)** | 24 | 46 | 51 | 85 | 96 | 5 | 3.6 |
| **$[Ag_2(pda)(PPh_3)_4]$ (25)** | 12 | 15 | 36 | 51 | 96 | 2.5 | 1.8 |
| **$[Ag(hxdaH)(PPh_3)_4].3H_2O$(26)** | 15 | 28 | 34 | 54 | 98 | 2.5 | 1.8 |
| **$[Ag_2(hpda)(PPh_3)_4].C_7H_8$ (27)** | 12 | 29 | 40 | 57 | 92 | 2.5 | 1.6 |
| **$[Ag(odaH)(PPh_3)_2].C_7H_8$(28)** | 15 | 19 | 28 | 35 | 50 | 1.0 | 1.1 |
| **$[Ag(ndaH)(PPh_3)_2]$ (29)** | 12 | 19 | 29 | 50 | 68 | 2.5 | 3.1 |
| **$[Ag_2(dda)(PPh_3)_4].H_2O$ (30)** | 16 | 18 | 35 | 50 | 64 | 2.5 | 1.7 |
| **$[Ag_2$ (udda) $(PPh_3)_3]$ (31)** | 15 | 28 | 34 | 56 | 69 | 2.5 | 2.1 |
| **$[Ag(dddaH)(PPh_3)_2]$(32)** | 16 | 28 | 37 | 50 | 96 | 2.5 | 2.9 |
| **$[Ag_2(uddca)(PPh_3)_5]$(33)** | 16 | 26 | 45 | 50 | 69 | 2.5 | 1.4 |
| **$[Ag(hxdaH)(PPh_3)_2].C_7H_8$ (34)** | 06 | 26 | 38 | 46 | 85 | 2.5 | 2.8 |
| **$[Ag_2(hpda)(PPh_3)_5].C_7H_8$ (35)** | 15 | 35 | 50 | 64 | 87 | 5.0 | 2.8 |
| **$[Ag_2(oda)(PPh_3)_4].2C_7H_8$ (36)** | 12 | 35 | 48 | 53 | 89 | 5.0 | 3.1 |
| **$Ag_2(udda)(PPh_3)_4]$ (37)** | 16 | 48 | 59 | 75 | 96 | 5.0 | 3.4 |
| **$[Ag_2(uddca)(PPh_3)_5].C_7H_8$(38)** | 12 | 56 | 85 | 96 | - | 10.0 | 5.3 |

***Table 40***: Anti-*Candida* activity and $IC_{50}$ values of dppm and dppe complexes **39-60**

| **Compound** | **% growth at concentration (µg /ml)** | | | | | | |
|---|---|---|---|---|---|---|---|
| | **20** | **10** | **5** | **2.5** | **1.0** | **$IC_{50}$ (µg /ml)** | **$IC_{50}$ (µM)** |
| **$[Ag_2(prda)(dppm)_3].C_7H_8$ (39)** | 16 | 22 | 35 | 45 | 56 | 1.0 | 0.9 |
| **$[Ag_2(bda)(dppm)_3].C_7H_8$ (40)** | 04 | 15 | 29 | 35 | 46 | 1.0 | 0.9 |
| **$[Ag_2(pda)(dppm)_4]$ (41)** | 06 | 15 | 38 | 47 | 75 | 2.5 | 2.2 |
| **$[Ag_2(hxda)(dppm)_4]$ (42)** | 08 | 25 | 37 | 45 | 68 | 2.5 | 2.1 |
| **$[Ag_2(hpda)(dppm)_4]$ (43)** | 09 | 35 | 46 | 58 | 72 | 2.5 | 2.1 |
| **$[Ag_2(oda)(dppm)_4]$ (44)** | 05 | 15 | 46 | 86 | - | 5.0 | 4.2 |
| **$[Ag_2(nda)(dppm)_4]$ (45)** | 16 | 28 | 58 | 95 | - | 5.0 | 4.1 |
| **$[Ag(ddaH)(dppm)_3].3H_2O$ (46)** | 15 | 25 | 35 | 46 | 50 | 1.0 | 1.0 |
| **$[Ag_2(udda)(dppm)_4]$(47)** | 12 | 16 | 28 | 35 | 50 | 1.0 | 0.8 |
| **$[Ag_2(ddda)(dppm)_4].H_2O$ (48)** | 24 | 56 | 69 | 73 | 85 | 10.0 | 7.9 |
| **$[Ag_2(uddca)(dppm)_4].2H_2O$ (49)** | 19 | 45 | 62 | 89 | 90 | 10.0 | 7.7 |
| **$[Ag_2(prda)(dppe)_4].H_2O$ (50)** | 12 | 25 | 30 | 46 | 59 | 2.5 | 2.1 |
| **$[Ag_2(bda)(dppe)_4]$ (51)** | 13 | 27 | 39 | 48 | 59 | 2.5 | 2.1 |
| **$[Ag_2(pda)(dppe)_3].4H_2O$ (52)** | 18 | 38 | 49 | 75 | 89 | 5.0 | 4.7 |
| **$[Ag_2(hxda)(dppe)_4]$ (53)** | 12 | 35 | 48 | 65 | 89 | 5.0 | 4.1 |
| **$[Ag_2(hpda)(dppe)_3]$ (54)** | 15 | 29 | 30 | 52 | 69 | 2.5 | 2.4 |
| **$[Ag_2(oda)(dppe)_4]$ (55)** | 16 | 38 | 46 | 86 | - | 5.0 | 4.0 |
| **$[Ag_2(nda)(dppe)_4].2H_2O$ (56)** | 17 | 29 | 56 | 66 | 85 | 5.0 | 3.9 |
| **$[Ag_2(dda)(dppe)_4]$ (57)** | 3 | 12 | 29 | 40 | 50 | 1.0 | 0.8 |
| **$[Ag_2(udda)(dppe)_4].H_2O$ (58)** | 6 | 18 | 29 | 34 | 46 | 1.0 | 0.7 |
| **$[Ag_2(ddda)(dppe)_4]$ (59)** | 9 | 16 | 18 | 29 | 48 | 1.0 | 0.8 |
| **$[Ag_2(uddca)(dppe)_4]$ (60)** | 26 | 37 | 52 | 75 | 89 | 5.0 | 3.8 |

***Table 41***: Anti-*Candida* activity and $IC_{50}$ values of Amp B and the free ligands (dicarboxylic acids, $PPh_3$, dppm and dppe)

| **Compound** | **% growth at concentration (µg /ml)** | | | | | | **$IC_{50}$ (µM)** |
|---|---|---|---|---|---|---|---|
| | **20** | **10** | **5** | **2.5** | **1.0** | **$IC_{50}$ (µg /ml)** | |
| **Amphotericin B** | 00 | 00 | 00 | 00 | 6 | 1.0 | 0.9 |
| **prda$H_2$** | 50 | 90 | - | - | - | 20.0 | 192 |
| **bda $H_2$** | 40 | 57 | - | - | - | 10.0 | 84 |
| **pda $H_2$** | 25 | 56 | - | - | - | 10.0 | 75 |
| **hxda $H_2$** | 38 | 48 | - | - | - | 10.0 | 68 |
| **hpda$H_2$** | 26 | 50 | - | - | - | 10.0 | 62 |
| **oda$H_2$** | 35 | 52 | - | - | - | 10.0 | 57 |
| **nda$H_2$** | 56 | 90 | - | - | - | 20.0 | 106 |
| **dda$H_2$** | 38 | 51 | - | - | - | 10.0 | 49 |
| **udda$H_2$** | 48 | 95 | - | - | - | 20.0 | 92 |
| **ddda$H_2$** | 50 | 94 | - | - | - | 20.0 | 86 |
| **uddca$H_2$** | 46 | 96 | - | - | - | 20.0 | 82 |
| **$PPh_3$** | 39 | 51 | - | - | - | 10.0 | 38 |
| **dppm** | 50 | 95 | - | - | - | 20.0 | 100 |
| **dppe** | 52 | 96 | - | - | | 20.0 | 93 |

The silver dicarboxylate complexes **1-11** exhibit potent anti-*Candida* activity at extremely low concentrations (1.0 μg/ml, 0.5 μg/ml, 0.25 μg/ml and 0.1 μg/ml) which compare favourably with the activities of $AgNO_3$ and [$Ag(CH_3COO)$] (Table 38).

Clearly the inclusion of the $PPh_3$ groups as auxiliary ligands in the silver complexes **12-38** has reduced their activity by between 10 and 100 times that of simple dicarboxylates **1-11**. These triphenylphosphine ($PPh_3$) derivatives of complexes **1-11** are all effectively inactive towards the *Candida albicans* at concentrations below 1μg/ml **(**Table 38). At 10 μg/ml these complexes are good to moderate antifungal agents and when the concentration is increased to 20 μg/ml the compounds all exhibit excellent activity (Table 39)

Like the $PPh_3$ derivatives the dppm and dppe complexes **39-60** are significantly less active than the simple silver carboxylate complexes **1-11** with their activity reduced by between 10 and 100 fold (Table 40). When compared to the $PPh_3$ complexes (**12-38**) the dppm and dppe derivatives show a similar activity profile at 20 μg/ml, 10 μg/ml and 5 μg/ml but when the concentration drops to 1μg/ml a number of the complexes are still moderately active (Table 39**)**. It is clear that the dppm and dppe derivatives have a concentration dependent activity profile and at 10 μg/ml and 20 μg/ml all of these compounds exhibit excellent activity towards the *Candida albicans.*

**D.7.3 Anti-bacterial activity of the complexes**

The antibacterial activity of complexes **1-60,** the free ligands and $AgNO_3$ against Grampositive and Gramnegative bacteria was determined over seven concentrations (50 μg /ml , 25 μg /ml, 10 μg /ml, 5 μg /ml, 2.5 μg /ml, 1 μg /ml and 0.1 μg /ml). The bacterial strains tested were (i) a clinical isolate of MRSA, (ii) *S. aureus* (ATCC 25922-as reference), (iii) a clinical isolate of *E. coli* and (iv) *E.coli* (ATCC 25923-as reference).

The experiments were carried out as described in the experimental section, each sample was tested in duplicate and each experiment was repeated three times. The results shown represent the average of these results. The majority of the complexes and all of the free ligands were found to be effectively inactive towards the pathogens over the concentration range tested. Table 42 lists the $IC_{50}$ values (μg/ml) for the 13 active complexes and the activities for $AgNO_3$.

$AgNO_3$ is a very potent antibacterial agent with a similar activity profile against the four test microbes. Of the simple silver dicarboxylates **1-11** only complexes **1, 4, 5, 6** and **7** exhibit significant activity. Of the $PPh_3$, dppm and dppe derivatives **12-60** only complexes **14**, **31**, **33**, **37**, **38, 39, 41** and **52** were found to be active.

Complexes **31**, **37** and **38** exhibit exceptional activity against the test microbes and have activity comparable to that of the silver nitrate.

***Table 42***: Anti-bacterial activity as $IC_{50}$ values of $AgNO_3$ and the complexes that exhibited activity

| Compound Code | ***S. aureus*** **ref. ATCC25923** | ***S.aureus*** **clinical (MRSA)** | ***E. coli*** **ref. ATCC25922** | ***E. coli*** **clinical** |
|---|---|---|---|---|
| **$AgNO_3$** | <0.1 | <0.1 | <0.1 | <0.1 |
| **$[Ag_2(prda)]$ (1)** | 15 | 13 | 38 | 18 |
| **$[Ag_2(hxda)]$ (4)** | 50 | 50 | 50 | 30 |
| **$[Ag_2(hpda)]$ (5)** | 8 | 30 | 8 | 4 |
| **$[Ag_2(oda)]$ (6)** | 6 | 8 | 6 | 8 |
| **$[Ag_2(nda)]$ (7)** | 8 | 10 | 12 | 10 |
| **$[Ag_2(pda)(PPh_3)_3].2H_2O$ (14)** | 30 | 12 | inactive | 15 |
| **$[Ag_2(udda)(PPh_3)]$ (31)** | <0.1 | <0.1 | <0.1 | <0.1 |
| **$[Ag_2(uddca)(PPh_3)_2]$ (33)** | 8 | 50 | 50 | 50 |
| **$[Ag_2(udda)(PPh_3)_4]$ (37)** | <0.1 | <0.1 | <0.1 | <0.1 |
| **$[Ag_2(uddca)(PPh_3)]$ (38)** | <0.1 | <0.1 | <0.1 | <0.1 |
| **$[Ag_2(prda)(dppm)_3].C_7H_8$ (39)** | * | 5 | 10 | * |
| **$[Ag_2(pda)(dppm)_4]$ (41)** | * | 12 | inactive | inactive |
| **$[Ag_2(pda)(dppe)_3].4H_2O$ (52)** | * | 18 | 28 | * |

The antimicrobial experiments carried out as part of this study have shown that all of the metal free dicarboxylic acids and phosphine based ligands are relatively poor antifungals and display no antibacterial activity. The simple dicarboxylate complexes **1-11** are potent in-vitro anti-*Candida* agents which display activity superior/comparable to the clinically used $AgNO_3$ and the state-of -the -art organic drug Amphothericin B. Indeed the majority of complexes **1-11** are twice as active as $AgNO_3$, which may arise

from the fact that they contain two silver ions per molecule. Therefore the assumption could be that they elute twice as many silver ions into the media than the simple silver nitrate salt. It has been reported that a higher dose of $AgNO_3$ was required to kill Gram positive (*S. aureus*) than Gramnegative (*E. coli*) cells. The authors claimed that this reflected the fact that the cell wall of the latter species was considerably thinner. In contrast, under the experimental conditions in which the present study was conducted the $AgNO_3$ is a potent antibacterial agent and did not discriminate in its activity against the Gram positive and Gram negative species. The antibacterial activity of the complexes **1-11** showed a surprising deviation from that of the simple silver salt. Indeed only five of the silver dicarboxylates (complexes **1, 4, 5, 6** and **7**) displayed good antibacterial activity, although it was significantly less than that of $AgNO_3$. Furthermore, unlike the $AgNO_3$ the activity of these five complexes displayed some discrimination in activity towards the Grampositive (*S. aureus* /MRSA) and Gram negative (*E.coli*) bacteria. Therefore, it is suggested that the silver dicarboxylate complexes **1-11** do not act on microbial cells in the same way as $AgNO_3$ and that the ligand must play some role in their mode of antimicrobial action contributing to their selectivity between antibacterial and antifungal activity.

Addition of the $PPh_3$ ligands to silver dicarboxylates **1-11** yielded the photo-stable complexes **12-38**. All 27 of these complexes exhibited significant antifungal activity against the *Candida albicans* cells although their activity is, on average, over ten times less than that of the equivalent silver dicarboxylate. This may reflect the relative stability of the $PPh_3$ derivatives which would not be expected to leach the silver ions easily. Of the 27 $PPh_3$ derivatives only complexes **14, 31, 33, 37** and **38** are active against the bacterial cells tested. Complex **14** is interesting as it displays no activity against the reference *E.coli* (ATCC 25922) cell line but is significantly effective at killing the clinical isolate. Complexes **31, 37** and **38** are the only complexes that display higher antibacterial activity than antifungal activity, a trend not previously observed for any silver based antimicrobials studied in this and collaborating laboratories. Indeed these complexes display antibacterial activity comparable to that of $AgNO_3$ but are very photostable, and over 20, 30 and 50 times (respectively) more active against the Grampositive and Gramnegative bacterial cells than the fungal cells. The fact that complexes **31, 37** and **38** did not manifest similar antifungal activity when

incubated with *C. albicans* suggests that their mode of action is not due simply to release of silver ions. The unique structure, which incorporates fatty dicarboxylic acid ligands {$^{-}$OOC-$(CH_2)_n$-$COO^{-}$ where n = 9 (complexes **31** and **37**) and 11 (complex **38**)} and the stablising phosphines, of these synthesised complexes may explain these observations. Due to cell wall differences, traditional prophylactic treatments differ for both bacterial and fungal infections. We propose, from this study, that the ligated structures passively diffused through the peptidoglycan cell wall of Grampositive bacterial and the lipopolysaccaride cell wall of Gramnegative bacteria. At this stage, it is difficult to elucidate definitely whether the complexes reached the targeted compartments of either the perisplasmic space or the cytoplasm. Furthermore, bacterial functional groups may exchange with ligands from the metallo-complexes, promoting silver ion discharge. Complexes **31, 37** and **38** represent potential therapeutics that warrent further investigation as novel antimicrobial agents. Further studies such as Graphite Furnace AAS (silver release determination), Raman (silver bonding) and Transmission Electron Spectroscopy (TEM, imaging of metal deposition) will help to clarify further the observed novel broad-spectrum properties of these three structures.

Addition of the dppm and dppe ligands to the silver dicarboxylates **1-11** yielded the photo-stable complexes **39-60** which all exhibited significant antifungal activity against the *Candida albicans* cells. However, with the exception of complex **39,** most of their activities are again significantly less than that of the equivalent silver dicarboxylate. Again this may reflect the relative stability of the dppm and dppe derivatives which would not be expected to leach the silver ions easily. Of the 22 diphosphine derivatives only complexes **39, 41** and **52** display any activity against the bacterial cells tested. Complex **41** is interesting as it exhibits good activity against the Grampositive MRSA but it is inactive against the Gramnegative *E.coli.* Complexes **39** and **52** display some discrimination in activity towards the Grampositive (MRSA) and Gramnegative (*E.coli*) bacteria. Again as all of the dppm and dppe derivatives **36-60** were found to be active against the fungal cells and only three of them displayed activity against MRSA and *E.coli* it is suggested that they do not act on microbial cells in the same way as $AgNO_3$ and that the ligands must play some role in their mode of antimicrobial action contributing to their selectivity between antibacterial and antifungal activity.

# EXPERIMENTAL

## E.1 INSTRUMENTATION

Infrared (IR) spectra were recorded in the region 400- 4000cm$^{-1}$ on a Nicolet FT-IR 400 Impact spectrometer. All solids to be tested were prepared in a KBr matrix.

*C. Albicans* cells were measured using a 20 Genesys Spectrophotometer. All solutions were prepared using 5 mls of Phosphate Buffer Saline (PBS).

Antimicrobial susceptibility testing was carried out using BIOTEC EL808 machine used for 96 well microtitreplate analysis.

Elemental analysis was carried out by the Microanalytical Laboratory, University College Dublin, Ireland.

X-ray crystal structures were carried out by Professor Vickie McKee, Loughborough University

## E.2 CHEMICALS

All chemicals were purchased from commercial sources and were used without further purification.

All reported solubility tests were carried out in hot solvent.

## E.3 SYNTHESIS OF SILVER (I) DICARBOXYLATE COMPLEXES

### E.3.1 [$Ag_2$(prda)] ($prdaH_2$= Propanedioic acid) (1)

The following procedure was conducted with the exclusion of all light sources. To a suspension of $prdH_2$ (0.261 g, 2.5 mmol) in 30 mls of Toluene, 0.834 g (0.5 mmol) of [$Ag(CH_3COO)$] was added and refluxed for two and half hours. At regular intervals of 30 mins the reflux condenser was removed for a minimum of five minutes to allow any acetic acid formed in the reaction to evaporate off. After two and half hours the heat was switched off and the mixture was left to stir for a further half an hour to cool down. The mixture was then filtered and the resulting precipitate was washed using small portions of toluene and 5-10 mls of diethyl ether and then air dried.

Yield: 0 .626 g (57.16%)

% Calc: C 11.34, H 0.63, Ag 67.89

% Found: C 11.32, H 0.64, Ag 65.01

Melting point: 132-136 ºC

IR (KBr): 3500, 2360, 1570, 1436, 1403, 1356, 1268, 1190, 668, 589 $cm^{-1}$.

Solubility: Not soluble in water, methanol, chloroform, acetone and DMSO.

### E.3.2 [$Ag_2$(bda)] ($bdaH_2$= Butanedioic acid) (2)

0.301g (2.55 mmol) of $bdaH_2$ in 30 mls of toluene reacted with 0.834 g (0.5 mmol) of [$Ag(CH_3COO)$].

Yield: 0.7336 g (64.63%).

% Calc: C 14.48, H 1.22, Ag 65.02

% Found: C 14.22, H 1.68, Ag 64.88

Melting point: 122-126 ºC

IR (KBr): 3428, 2349, 1655, 1566, 1410, 1296, 1019, 925, 652, 420$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in methanol, chloroform, acetone and DMSO.

### E.3.3 [$Ag_2$(pda)] ($PdaH_2$= Pentanedioic acid) (3)

0.336 g (2.55 mmol) of $pdaH_2$ in 30mls of toluene reacted with 0.834 g (0.5 mmol) of [$Ag(CH_3COO)$].

Yield : 0.5063 g (43.27%).

% Calc: C 17.36, H 1.75, Ag 62.38

% Found: C 17.22, H 1.6, Ag 63.06

Melting point: 128-133 ºC

IR (KBr): 3405, 2959, 2362, 1589, 1400, 1314, 1065, 912, 738, 601$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in methanol, chloroform, acetone and DMSO.

### E.3.4 [$Ag_2$(hxda)] (hxda$H_2$= Hexanedioic acid) (4)

0.372 g (2.55 mmol) of hxda$H_2$ in 30 mls of toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)].

Yield: 0.8710 g (72.22%).

% Calc: C 20.03, H 2.24, Ag 59.95

% Found: C 20.59, H 2.16, Ag 58.67

Melting point: 128-132 ºC

IR (KBr): 3419, 2925, 1650, 1564, 1409, 1199, 1019, 925, 737, 652$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in methanol, chloroform, acetone and DMSO.

### E.3.5 [$Ag_2$(hpda)] (hpda$H_2$=Heptanedioic acid) (5)

0.408 g (2.55 mmol) of hpda$H_2$ in 30 mls of Toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.5768 g (46.44%)

% Calc: C 22.49, H 2.7, Ag 57.70

% Found: C 22.43, H 2.26, Ag 57.89

Melting point: 131-135 ºC

IR (KBr): 3419, 2933, 2349, 1651, 1564, 1407, 654$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in methanol, chloroform, acetone and DMSO.

### E.3.6 [$Ag_2$(oda)] (oda$H_2$= Octanedioic acid) (6)

0.444 g (2.55 mmol) of oda$H_2$ in 30 mls of toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.6624 g (51.83%).

% Calc: C 24.77, H 3.12, Ag 55.61

% Found: C 24.27, H 3.17, Ag 55.31

Melting point: 128-132 ºC

IR (KBr): 2930, 1653, 1566, 1409, 1285, 1192, 1018, 922, 791, 718, 651$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in methanol, chloroform, acetone and DMSO.

**E.3.7 [$Ag_2$(nda)](nda$H_2$= Nonanedioic acid) (7)**

0.470 g (2.5 mmol) of nda$H_2$ in 30mls of toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.774 g (59.35%).

% Calc: C 26.89, H 3.51, Ag 53.67

% Found: C 26.39, H 3.01, Ag 53.41

Melting point: 130-135 ºC

IR (KBr): 3396, 2933, 1689, 1567, 1463, 1408, 1287, 1200, 1017, 916, 736$cm^{-1}$.

Solubility: Partially soluble in water, not soluble in, methanol, chloroform, acetone and DMSO.

**E.3.8 [$Ag_2$(dda)] (dda$H_2$= Decanedioic acid) (8)**

0.515 g (2.55 mmol) of dda$H_2$ in 30mls of toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.857 g (63.52%).

% Calc: C 28.87, H 3.88, Ag 51.86

% Found: C 28.11, H 3.5, Ag 52.01

Melting point: 127-132 ºC

IR (KBr): 3417, 2929, 1679, 1567, 1471, 1408, 1257, 1188, 1018, 924, 753$cm^{-1}$.

Solubility: Not soluble in water, methanol, chloroform, acetone and DMSO.

**E.3.9 [$Ag_2$(udda)] (udda$H_2$= Undecanedioic acid) (9)**

0.541g (2.5 mmol) of udda$H_2$ in 30mls of toluene reacted with 0.834 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.9469 g ( 68.86%)

% Calc: C 28.87, H 3.66, Ag 50.17

% Found: C 28.34, H 3.84, Ag 50.77

Melting point: 133-138 ºC

IR (KBr): 3407.49, 2929.42, 2913.25, 2846.61, 1584.90, 1466.37, 1409.26, 1315.53, 1251.31, 721.30 $cm^{-1}$.

Solubility: Partially soluble in DMSO, insoluble in methanol, ethanol, chloroform, acetone and water.

### E.3.10 [$Ag_2$(ddda)] (ddda$H_2$= Dodecanedioic acid) (10)

0.587 g (2.55 mmol) of ddda$H_2$ in 30 mls of toluene reacted with 0.834g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.5163 g (36.33%).

% Calc: C 32.46, H 4.54, Ag 48.59

% Found: C 32.22, H 4.94, Ag 48.83

Melting point: 134-138 ºC

IR (KBr): 3417, 2910, 1688, 1567, 1470, 1408, 1230, 1186, 1018, 923, 651$cm^{-1}$.

Solubility: Not soluble in water, methanol, chloroform, acetone and DMSO.

### E.3.11 [$Ag_2$(uddca)] (uddca$H_2$= Undecanedicarboxylic acid) (11)

0.623 g (2.55 mmol) of uddca$H_2$ in 30 mls of toluene reacted with 0.8345 g (0.5 mmol) of [Ag($CH_3COO$)]

Yield: 0.787 g (54.01%)

% Calc: C 34.09, H 4.84, Ag 47.10

% Found: C 34.44, H 4.77, Ag 47.67

Melting point: 131-136 ºC

IR (KBr): 3417, 2917, 1693, 1562, 1467, 1409, 1272, 1229, 1110, 1019, 921$cm^{-1}$.

Solubility: Not soluble in water, methanol, chloroform, acetone and DMSO.

## E.4 SYNTHESIS OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$)

### E.4.1 $[Ag(prdaH)(PPh_3)_2]$ (12)

The following procedure was conducted with the exclusion of all light sources. To a conical flask containing a suspension of $PPh_3$ (0.669 g, 2.5 mmol) in 30ml of toluene, 0.319 g (1.0 mmol) of $[Ag_2(prda)]$ was added. The flask was then refluxed for two and half hours and left to stand for a further half an hour at room temp, allowing the mixture to cool. The solution was then filtered off and the resulting precipitate was washed using small portions of toluene and 5-10 ml of diethyl ether and then air dried. The flask containing the filtrate, were covered with foil and crystals were deposited over several weeks.

Yield: 0.7001 g (70.81%)

% Calc: C 63.69, H 4.52, P 8.42, Ag 14.67

% found: C 64.49, H 4.61, P 7.22, Ag 14.00

Melting point: 126-131 ºC

IR (KBR): 3053.46, 2923.84, 1730.96, 1598.67, 1548.18, 1478.65, 1434.16, 1402.56, 1370.28, 1181.33, 1158.16, 1095.67, 1070.46, 1026.96, 997.43, 891.95, 753.18, 694.60, 514.71, 494.09, 466.66, 441.58$cm^{-1}$.

Solubility: Partially soluble in methanol, ethanol, DMSO, acetone, chloroform, insoluble in water.

This procedure was used to generate all of the $PPh_3$ derivative of complexes **1-11** (using 2.5, 4 and 6 equivalents of phosphine ligands)

### E.4.2 $[Ag_2(bda)(PPh_3)_3].C_7H_8$ (13)

0.334 g (1.0 mmol) of $[Ag_2(bda)]$ in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.7946 g (79.24%)

% Calc: C 64.48, H 4.74, P 7.67, Ag 17.82

% found: C 64.98 , H 4.98, P 7.89, Ag 18.53

Melting point: 132-137 ºC

IR (KBR): 3053.28, 2962.96, 2921.08, 1644.58, 1549.09, 1478.64, 1434.22, 1393.12, 1306.32, 1275.43, 1182.74, 1156.90, 1095.27, 1068.93, 1027.80,

995.96, 888.28, 798.64, 768.78, 745.25, 705.52, 693.43, 618.01, 501.49, 432.40cm$^{-1}$.

Solubility**:** Partially soluble in chloroform insoluble in water, methanol, ethanol, acetone, DMSO.

### E.4.3 [$Ag_2(pda)(PPh_3)_3$].2$H_2O$ (14)

0.348 g (1.0 mmol) of [$Ag_2$(pda)] in 30mls of toluene reacted with 0.669g (2.5 mmol) of $PPh_3$.

Yield: 0.4820 g (47.40%)

% Calc: C 60.63, H 4.74, P 7.95, Ag 18.46

% found: C 60.51, H 4.43, P 7.86, Ag 18.87

Melting point: 129-134 ºC

IR (KBR): 3052.53, 2962.66, 2920.86, 1961.23, 1887.41, 1816.34, 1770.72, 1633.75, 1571.00, 1548.82, 1478.78, 1434.22, 1392.67, 1345.85, 1306.33, 1275.60, 1182.99, 1156.95, 1095.36, 1069.26, 1027.86, 996.14, 942.38, 917.18, 888.71, 848.54, 798.90, 768.99, 745.26, 705.47, 693.62, 618.17, 501.76, 432.29 cm$^{-1}$.

Solubility: insoluble in water, acetone soluble in methanol, ethanol, chloroform, DMSO.

### E.4.4 [$Ag_2(hxda)(PPh_3)_2$] (15)

0.362 g (1.0mmol) of $Ag_2$(hxda) in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$

Yield: 0.4178 g (40.53%)

% Calc: C 57.04, H 4.33, P 7.00, Ag 24.34

% found: C 57.04, H 4.30, P 6.43, Ag 22.89

Melting point: 133-138 ºC

IR (KBR): 3049.25, 2934.11, 2892.38, 1620.02, 1552.16, 1478.59, 1459.58, 1435.04, 1414.08, 1365.95, 1309.41, 1193.33, 1095.25, 1071.67, 1025.28, 997.49, 912.48, 758.21, 746.58, 693.08, 520.36, 505.50, 496.15, 444.96 cm$^{-1}$

Solubility: Partially soluble in methanol, ethanol, DMSO, acetone, chloroform, water.

**E.4.5 $[Ag_2(hpda)(PPh_3)_2].2H_2O$ (16)**

0.376 g (1.0 mmol) of $[Ag_2(hpda)]$ in 30 mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.3099 g (29.68%)

% Calc: C 61.12, H 5.13, P 7.75, Ag 23.09

% found: C 61.60, H 4.87, P 7.27, Ag 23.00

Melting point: 130-135 ºC

IR (KBR): 3052.54, 2941.03, 2856.28, 2360.29, 1965.48, 1893.97, 1822.77, 1646.76, 1548.69, 1496.47, 1478.45, 1463.42, 1400.42, 1330.85, 1309.22, 1264.68, 1217.31, 1182.73, 1157.75, 1094.35, 1069.35, 1026.56, 996.26, 973.24, 917.26, 851.32, 748.28, 694.52, 655.38, 617.80, 514.46, 503.93, 466.61, 439.04 $cm^{-1}$.

Solubility: insoluble in water, ethanol, acetone, DMSO, partially soluble in chloroform, methanol.

**E.4.6 $\{[Ag_2(oda)(PPh_3)_3].2H_2O\}$ (17)**

0.390 g (1.0 mmol) of $[Ag_2(oda)]$ in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.649 g (61.35%)

% Calc: C 61.40, H 5.24, P 7.66, Ag 17.82

% found: C 61.02, H 5.07, P 7.44, Ag 17.34

Melting point: 131-136 ºC

IR (KBR): 3053.39, 2930.54, 2851.22, 2349.98, 2284.60, 1593.34, 1570.17, 1479.36, 1434.64, 1407.48, 1361.56, 1337.93, 1309.06, 1285.20, 1256.11, 1180.50, 1155.62, 1095.73, 1026.54, 996.84, 746.56, 693.60, 665.85, 618.58, 515.18, 499.60 $cm^{-1}$.

Solubility: insoluble in water, ethanol, partially soluble in methanol, acetone, chloroform and DMSO.

**E.4.7 $[Ag(ndaH)(PPh_3)_2]$ (18)**

0.404 g (1.0 mmol) of $[Ag_2(nda)]$ in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$

Yield: 0.578 g (53.91% )

% Calc: C 65.94, H 5.53, P 7.56, Ag 13.16

% found: C 65.67, H 5.01, P 7.88, Ag 12.96

Melting point: 127-132 ºC

IR (KBR): 2929.70, 2852.90, 2359.54, 1689.02, 1574.72, 1471.55, 1430.12,1405.66, 1344.10, 1273.17, 1232.96, 1193.77, 1098.25, 923.18, 904.06, 775.05, 719.11, 696.09, 539.67 $cm^{-1}$ .

Solubility: insoluble in water, partially soluble in methanol, ethanol, acetone, chloroform and DMSO.

**E.4.8 $[Ag_2(dda)(PPh_3)_4].2C_7H_8$ (19)**

0.418 g (1.0 mmol) of $[Ag_2(dda)]$ in 30 mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.7142 g (65.71%)

% Calc: C 69.82 , H 5.74, P7.50, Ag 12.86

% found: C 69.23, H 5.21, P 7.58, Ag 12.73

Melting point: 133-138 ºC

IR (KBR): 3051.98, 2923.75, 2849.14, 2359.49, 1893.40, 1714.21, 1597.09, 1569.64, 1479.67, 1466.11, 1434.47, 1407.79, 1357.90, 1307.97, 1267.09, 1236.04, 1186.45, 1156.84, 1096.38, 1070.92, 1027.06, 997.26, 916.34, 849.91, 753.70, 744.53, 694.60, 513.41, 502.11, 437.27 $cm^{-1}$.

Solubility: partially soluble in water methanol, ethanol, acetone, chloroform and DMSO.

**E.4.9 $[Ag_2(udda)(PPh_3)_2]$ (20)**

0.432 g (1.0 mmol) of $[Ag_2(udda)]$ in 30 mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.6402 g (58.15%)

% Calc: C 58.01, H 5.32 , P 6.63, Ag 22.60

% Found: C 59.46, H 5.00, P 6.63, Ag 22.38

Melting point: 126-131 ºC

IR (KBr): 3439.02, 3051.26, 2924.10, 2850.86, 1603.12, 1560.08, 1480.48, 1434.26, 1406.48, 1434.26, 1406.40, 1364.38, 1258.71, 1096.14, 744.65, 694.38, 520.06, 502.42 $cm^{-1}$.

Solubility: Partially soluble in chloroform and DMSO, insoluble in methanol, acetone, water, ethanol.

**E.4.10 [$Ag_2$(ddda)($PPh_3$)$_3$] (21)**

0.446 g (1.0 mmol) of [$Ag_2$(ddda)] in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.4967 g (45.70%)

% Calc: C 64.40, H 5.33, P 7.55, Ag 17.53

% found: C 64.55, H 5.53, P 7.43, Ag 17.23

Melting point: 128-133 ºC

IR (KBR): 3053.06, 2955.07, 2927.15, 2677.98, 2359.55, 2341.68, 1965.49, 1893.38, 1822.16, 1770.71, 1668.20, 1569.99, 1543.87, 1478.82, 1434.38, 1387.95, 1328.69, 1309.81, 1268.46, 1182.19, 1157.05, 1096.02, 1070.55, 1027.25, 996.89, 971.96, 914.78, 876.29, 850.42, 807.43, 744.97, 694.70, 660.08, 617.89, 513.15, 493.70, 439.68 $cm^{-1}$.

Solubility: insoluble in water, partially soluble in methanol, ethanol, acetone, chloroform, DMSO.

**E.4.11 [Ag(uddcaH)($PPh_3$)$_2$] (22)**

0.460 g (1.0 mmol) of [$Ag_2$(uddca)] in 30mls of toluene reacted with 0.669 g (2.5 mmol) of $PPh_3$.

Yield: 0.487 g (43.13%)

% Calc: C 67.20, H 6.10, P 7.07, Ag 12.32

% found: C 66.83, H 6.02, P 7.31, Ag 12.45

Melting point: 134-138 ºC

IR (KBR): 3053,921, 2849, 1703, 1561, 1478, 1402, 1258, 1095, 996, 618, 523, 444 $cm^{-1}$.

Solubility: insoluble in water, partially soluble in methanol, ethanol, acetone, chloroform, DMSO.

## E.5 SYNTHESIS OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$)

### E.5.1 $[Ag_2(prda)(PPh_3)_3].H_2O$ (23)

0.319 g (1.0 mmol) of $[Ag_2(prda)]$ in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.681 g (49.85%)

% Calc: C 60.98, H 4.4, P 8.28, Ag 19.22

% Found: C 60.95, H 4.29, P 8.18, Ag 19.22

Melting point: 132-137 ºC

IR (KBr): 3427, 1602, 1546, 1477, 1432, 1317, 1093, 1030, 983, 742, 694, 579, 514, 493 $cm^{-1}$

Solubility: Partially soluble in water, chloroform, methanol and DMSO. Not soluble in acetone.

### E.5.2 $[Ag_2(bda)(PPh_3)_4]$ (24)

0.334 g (1.0 mmol) of $[Ag_2(bda)]$ in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.9561 g (69.13%)

% Calc: C 66.1, H, 4.67, P 8.97, Ag 15.62

% Found: C 66.05, H, 4.76, P 8.44, Ag 15.53

Melting point: 131-136 ºC

IR (KBr): 3441, 3052, 1542, 1477, 1433, 1386, 1179, 1093, 1026, 995, 913, 743, 693, 659, 507, 491, 441$cm^{-1}$.

Solubility: Partially soluble in chloroform, methanol, acetone and DMSO, not soluble in water.

### E.5.3 $[Ag_2(pda)(PPh_3)_4]$ (25)

0.348 g (1.0 mmol) of $[Ag_2(pda)]$ in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.6251 g (44.74%)

% Calc: C 66.3, H 4.77, P 8.88, Ag 15.47

% Found: C 66.96, H 4.75, P 8.88, Ag 15.83

Melting point: 130-135 ºC

IR (KBr): 3050, 1548, 1477, 1433, 1391, 1305, 1094, 1023, 990, 798, 743, 692, 499 $cm^{-1}$.

Solubility: Partially soluble in water, chloroform and methanol, not soluble in acetone and DMSO.

### E.5.4 $[Ag(hxdaH)(PPh_3)_3].3H_2O$ (26)

0.362 g (1.0 mmol) of $[Ag_2(hxda)]$ in 30mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.6425 g (45.53%)

% Calc: C 65.88, H 5.53, P 8.49, Ag 9.86

% Found: C 65.22, H, 4.98, P 8.39, Ag 9.12

Melting point: 126-131 ºC

IR (KBr): 3053, 3931, 1708, 1572, 1551, 1478, 1434, 1395, 1310, 1246, 1095, 1026, 996, 745, 693, 612, 512, 501, 426 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

### E.5.5 $[Ag_2(hpda)(PPh_3)_4].C_7H_8$ (27)

0.376 g (1.0 mmol) of $[Ag_2(hpda)]$ in 30mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.7753 g (54.40%)

% Calc: C 68.17, H 5.19, P 8.18, Ag 14.24

% Found: C 68.72, H 5.20, P 8.14, Ag 14.77

Melting point: 127-132 ºC

IR (KBr): 3433, 3048, 1546, 1477, 1433, 1393, 1308, 1093, 1025, 994, 883, 837, 747, 692, 503 $cm^{-1}$.

Solubility: Partially soluble in water, chloroform, methanol, acetone and DMSO.

### E.5.6 $[Ag(odaH)(PPh_3)_2].C_7H_8$ (28)

0.390 g (1.0 mmol) of $[Ag_2(oda)]$ in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.8449 g (58.71%)

% Calc: C 68.23, H 5.73, P 6.90, Ag 12.02

% Found: C 69.96, H 5.43, P 7.86, Ag 12.34

Melting point: 128-132 ºC

IR (KBr): 2920, 2851, 1704, 1583, 1546, 1494, 1478, 1433, 1399, 1254, 1180, 1156, 1094, 1025, 995, 746, 694, 515, 493, 417 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**Note:** Crystals of 28 deposited when the mother liquor was allowed to stand for several weeks.

### E.5.7 [Ag(ndaH)($PPh_3$)$_2$]. (29)

0.404 g (1.0 mmol) of [$Ag_2$(nda)] in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.7992 g (55.00%)

% Calc: C 65.94, H 5.53, P 7.56, Ag 13.16

% Found: C 65.59, H 4.92, P 8.71, Ag 13.87

Melting point: 129-134 ºC

IR (KBr): 3053, 2931, 2360, 2341, 1700, 1572, 1550, 1478, 1434, 1389, 1312, 1095, 1026, 996, 911, 744, 705, 693, 668, 503, 427$cm^{-1}$.

Solubility: Partially soluble in chloroform, methanol, acetone and DMSO, not soluble in water.

### E.5.8 [$Ag_2$(dda)($PPh_3$)$_4$].$H_2O$ (30)

0.418 g (1.0 mmol) of [$Ag_2$(dda)] in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

Yield: 0.7499 g (51.11%)

% Calc: C 66.41, H 5.3, P 8.35, Ag 14.28

% Found: C 66.05, H 5.66, P 8.47, Ag 14.89

Melting point: 130-135 ºC

IR (KBr): 3442, 3051, 2921, 2849, 2360, 1635, 1478, 1433, 1282, 1180, 1095, 1027, 995, 752, 693, 512, 499 $cm^{-1}$.

Solubility: Partially soluble in water, chloroform, methanol and acetone, not soluble in DMSO.

**E.5.9 [$Ag_2$(udda)($PPh_3$)$_3$] (31)**

0.432 g (1.0 mmol) of [$Ag_2$(udda)] in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$

Yield: 0.5171g (34.91%)

% Calc: C 64.16, H 5.22, P 7.64, Ag 17.73

% Found: C 64.52, H 5.03, P 7.69, Ag 17.86

Melting point: 131-136 ºC

IR (KBr): 3441.02, 3050.80, 2922.24, 2852.36, 1556.15, 1479.38, 1433.11, 1394.80, 1304.04, 1183.92, 1157.17, 1094.59, 1068, 1027.29, 997.18, 743.29, 693.62, 617.78, 512.73, 503.19, 438.61$cm^{-1}$.

Solubility: Insoluble in methanol, chloroform, ethanol, acetone, DMSO and water.

**Note:** Crystals of **[$Ag_2$ (udda)($PPh_3$)$_4$](31A)** deposited from the mother liquor after it was left standing for several weeks.

**E.5.10 [$Ag_2$(dddaH)($PPh_3$)$_3$] (32)**

0.446 g (1.0 mmol) of [$Ag_2$(ddda)] in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$.

[Ag(dddaH)($PPh_3$)$_3$] **32** deposited, in very low yield, as crystals. The formulation is based on the X-ray crystallographic analysis.

**E.5.11 [$Ag_2$(uddcaH)($PPh_3$)$_2$] (33)**

0.460 g (1.0 mmol) of [$Ag_2$(udda)] in 30 mls of toluene reacted with 1.049 g (4.0 mmol) of $PPh_3$. [Ag(uddcaH)($PPh_3$)$_2$] **33** deposited in very low yield as crystals. The formulation is based on the x-ray crystallographic analysis.

## E.6 SYNTHESIS OF SILVER (I) DICARBOXYLATE COMPLEXES WITH TRIPHENYLPHOSPHINE ($PPh_3$)

### E.6.1 $[Ag_2(prda))(PPh_3)_3].H_2O$ (23)

0.319 g (1.0 mmol) of $[Ag_2(prda)]$ in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 0.8479 g (44.79%)

% Calc: C 60.98, H 4.40, P 8.28, Ag 19.22

% Found: C 62.97, H 4.47, P 8.41, Ag 19.76

Melting point: 132-137 ºC

IR (KBr): 3051, 1545, 1477, 1432, 1317, 1182, 1093, 1023, 990, 742, 694, 579, 514, 493 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

### E.6.2 $[Ag_2(bda)(PPh_3)_4]$(24)

0.334 g (1.0 mmol) of $[Ag_2(bda)]$ in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 1.0701 g (56.08%)

% Calc: C 66.1, H 4.67, P 8.97, Ag 15.62

% Found: C 66.59, H 4.77, P 9.07, 15.01

Melting point: 133-138 ºC

IR (KBr): 3052, 1543, 1477, 1433, 1387, 1308, 1093, 1025, 995, 910, 744, 659, 503 $cm^{-1}$.

Solubility: Partially soluble in chloroform, methanol, acetone and DMSO, not soluble in water.

### E.6.3 $[Ag_2(pda)(PPh_3)_4]$ (25)

0.348 g (1.0 mmol) of $[Ag_2(pda)]$ in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 0.9519 g (49.52%)

% Calc: C 66.30, H 4.77, P 8.88, Ag 15.47

% Found: C 65.74, H 4.75, P 8.71, Ag 15.33

Melting point: 134-138 ºC

IR (KBr): 3050, 1548, 1477, 1433, 1391, 1305, 1181, 1094, 1027, 994, 888, 743, 705, 692, 500, 431cm$^{-1}$.

Solubility: Partially soluble in chloroform, methanol, ethanol, DMSO, insoluble in acetone and water.

**E.6.4 [$Ag_2$(hxdaH)($PPh_3$)$_2$].$C_7H_8$ (34)**

0.362 g (1.0 mmol) of [$Ag_2$(hxda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 1.311 g (67.71%)

% Calc: C 64.87, H 5.06, P 7.97, Ag 22.07

% Found: C 64.78, H 5.13, P7.80, Ag 22.76

Melting point: 126-131 ºC

IR (KBr): 2922, 1723, 1547, 1478, 1434, 1397, 1309, 1242, 1095, 1026, 995, 745, 694, 440 cm$^{-1}$.

Solubility: Partially soluble in chloroform, methanol, ethanol, DMSO, insoluble in acetone and water.

**E.6.5 [$Ag_2$(hpda)($PPh_3$)$_5$].$C_7H_8$ (35)**

0.376 g (1.0 mmol) of [$Ag_2$(hpda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 1.401g (71.84%)

% Calc: C 70.28, H 5.27, P 8.71, Ag 12.14

% Found: C 70.64, H 5.17, P 9.67, Ag 12.86

Melting point: 127-132 ºC

IR (KBr): 3045, 1585, 1555, 1478, 1433, 1381, 1080, 1023, 994, 742, 692, 510, 434 cm$^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**E.6.6 [$Ag_2$(oda)($PPh_3$)$_4$].2$C_7H_8$ (36)**

0.390 g (1.0 mmol) of [$Ag_2$(oda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$

Yield: 1.3786 g (70.19%)

% Calc: C 69.63, H 5.47, P 7.64, Ag 13.31

% Found: C 69.02, H 5.44, P 7.86, Ag 13.66

Melting point: 128-133 ºC

IR (KBr): 3054, 2921, 2851, 1546, 1478, 1434, 1399, 1308, 1095, 1026, 996, 746, 694, 515, 504, 493,466, 418$cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**E.6.7 [Ag(ndaH)($PPh_3$)$_2$] (29)**

0.404 g (1.0 mmol) of [$Ag_2$(nda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$

Yield: 1.206 g (60.97%)

% Calc: C 65.94, H 5.53, P 7.56, Ag 13.16

% Found: C 65.59, H 4.92, P 8.71, Ag 13.91

Melting point: 129-134 ºC

IR (KBr): 3053, 2931, 1701, 1550, 1572, 1478, 1434, 1389, 1313, 1247, 1095, 1026, 996, 911, 744, 693, 612, 503, 427 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**E.6.8 [$Ag_2$(dda)($PPh_3$)$_4$].$H_2O$ (30)**

0.418 g (1.0 mmol) of [$Ag_2$(dda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$.

Yield: 1.298 g (65.16%)

% Calc: C 66.41, H 5.3, P 8.35, Ag 14.55

% Found: C 66.05, H 5.66, P 8.47, Ag 14.67

Melting point: 130-135 ºC

IR (KBr): 3051, 2921, 2849, 1701, 1635, 1478, 1433, 1309, 1180, 1095, 1027, 995, 752, 693, 499 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**E.6.9 [$Ag_2$(udda)($PPh_3$)$_4$] (37)**

0.432 g (1.0 mmol) of [$Ag_2$(udda)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$

Yield: 1.364 g (67.99%)

% Calc: C67.40, H 5.32, P 8.38, Ag 14.59

% Found: C 67.28, H 5.27, P 8.51, Ag 14.99

Melting point: 131-136 ºC

IR (KBr): 3051, 2923, 2852, 1556, 1479, 1433, 1395, 1304, 1094, 1027, 743, 693, 512, 503, 438 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**E.6.10 [$Ag_2$(uddca)($PPh_3$)$_5$].$C_7H_8$ (38)**

0.460 g (1.0 mmol) of [$Ag_2$(uddca)] in 30 mls of toluene reacted with 1.574 g (6.0 mmol) of $PPh_3$

Yield: 1.134 g (55.75%)

% Calc: C70.97, H 5.69, P 8.32, Ag 11.59

% Found: C 70.87, H 5.57, P 9.03, Ag 11.34

Melting point: 132-137ºC

IR (KBr): 3051, 2918, 2846, 1563, 1433, 1476, 1380, 1307, 1178, 1091, 1068, 1026, 996, 742, 617, 512, 420 $cm^{-1}$.

Solubility: Partially soluble in chloroform and methanol, not soluble in water, acetone and DMSO.

**Note :** Crystals of [$Ag_2$(uddca)($PPh_3$)$_6$] **38A** deposited from the mother liquor when it was left to stand for several weeks.

## E.7 SYNTHESIS OF SILVER DIPHENYLPHOSPHINEMETHANE COMPLEXES

### E.7.1 $[Ag_2(prda)(dppm)_3].C_7H_8$ (39)

0.319 g (1.0 mmol) of $[Ag_2(prda)]$ in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of Dppm.

Yield: 0.9759 g (89.77%)

% Calc: C 58.24, H 4.89, P 9.19, Ag 21.35

% Found: C 58.72, H 4.50, P 9.98, Ag 21.09

Melting point: 133-138 ºC

IR (KBr): 3644.35, 3426.46, 3049.19, 1592.27, 1537.01, 1483.35, 1434.77, 1336.15, 1241.36, 1164.94, 1100.61, 1025.67, 998.26, 910.64, 794.44, 737.94, 720.35, 692.76, 515.46, 503.81, 480.05 $cm^{-1}$.

Solubility: Partially soluble in methanol, ethanol, DMSO, acetone, chloroform, insoluble in water

### E.7.2 $[Ag_2(bda)(dppm)_3].C_7H_8$ (40)

0.334 g (1.0 mmol) of $[Ag_2(bda)]$ in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of Dppm.

Yield: 0.9164 g (83.15%)

% Calc: C 58.61, H 5.02, P 9.07, Ag 21.06

% Found: C 57.40, H 4.31, P 9.97, Ag 21.88

Melting point: 126-131 ºC

IR (KBr): 3660.25, 3426.30, 3052.71, 1547.11, 1483.81, 1435.41, 1385.50, 1100.09, 1000.04, 760.31, 736.84, 722.32, 693.77, 515.13, 480.51, 428.83 $cm^{-1}$.

Solubility: insoluble in methanol, partially soluble in water, ethanol, acetone, chloroform and DMSO

### E.7.3 $[Ag_2(pda)(dppm)_4]$ (41)

0.348 g (1.0 mmol) of $[Ag_2(pda)]$ in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of Dppm.

Yield: 0.9236 g (82.75%)

% Calc: C 59.05, H 4.87, P 11.08, Ag 18.81

% Found: C58.07, H 4.47, P 10.41, Ag 18.91

Melting point: 127-132 ºC

IR (KBr): 3432.35, 3050.34, 1557.02, 1483.46, 1435.28, 1382.45, 1100.70, 737.47, 696.16, 515.68, 480.30 $cm^{-1}$.

Solubility: insoluble in water, ethanol, acetone, DMSO, partially soluble in methanol, chloroform

**E.7.4 [$Ag_2$(hxda)(dppm)$_4$] (42)**

0.362 g (1.0 mmol) of [$Ag_2$(hxda)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of Dppm.

Yield: 0.580 g (51.32%)

% Calc: C 60.02, H 5.21, P 10.67, Ag 18.59

% Found: C 59.00, H 4.66 , P10.26, Ag 18.83

Melting point: 128-133 ºC

IR (KBr): 3434.27, 3049.86, 2922.70, 1555.25, 1483.83, 1436.18, 1390.71, 1311.50, 1142.58, 1100.20, 999.14, 784.56, 739.88, 720.78, 694.84, 516.29, 479.92 $cm^{-1}$.

Solubility: partially soluble in ethanol, DMSO, chloroform, insoluble in methanol, water, acetone.

**E.7.5 [$Ag_2$(hpda)(dppm)$_4$] (43)**

0.376 g (1.0 mmol) of [$Ag_2$(hpda)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.9505 g (83.08%)

% Calc: C 60.32, H 5.32, P 10.55, Ag 18.36

% Found: C 59.46, H 4.65, P 11.02, Ag 18.78

Melting point: 129-134 ºC

IR (KBr): 3424.14, 3050.37, 2937.01, 1559.41, 1483.63, 1435.27, 1395.44, 1099.57, 1026.34, 999.10, 737.88, 720.10, 693.84, 515.35, 480.02$cm^{-1}$.

Solubility: insoluble in water, ethanol, acetone, partially soluble in methanol, chloroform and DMSO

**E.7.6 [$Ag_2$(oda)(dppm)$_4$] (44)**

0.390 g (1.0 mmol) of [$Ag_2$(oda)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.689 g (59.49%)

% Calc: C 60.62, H 5.43, P 10.42, Ag 18.15

% Found: C 60.47, H 4.99, P 10.00, Ag 18.76

Melting point: 130-135 ºC

IR (KBr): 3432.58, 3050.99, 2940.41, 1560.87, 1484.33, 1435.37, 1389.85, 1100.00, 999.47, 740.40, 722.41, 694.79, 515.93, 482.32 $cm^{-1}$.

Solubility: insoluble in water, partially soluble in methanol, ethanol, acetone, chloroform and DMSO

**E.7.7 [$Ag_2$(nda)(dppm)$_4$] (45)**

0.404 g (1.0 mmol) of [$Ag_2$(nda)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.9435 g (80.50%)

% Calc: C 60.91, H 5.53, P 10.30, Ag 17.94

% Found: C 59.67, H 4.93, P 10.82, Ag 17.62

Melting point: 131-136 ºC

IR (KBr): 3426.72, 3051.37, 2929.90, 1553.79, 1483.62, 1435.34, 1392.50, 1099.21, 999.16, 740.87, 721.31, 693.97, 514.83, 480.77 $cm^{-1}$.

Solubility: partially soluble in water methanol, ethanol, acetone, chloroform and DMSO

**E.7.8 [Ag(ddaH)(dppm)$_3$].3$H_2O$ (46)**

0.418 g (1.0 mmol) of [$Ag_2$(dda)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.5925 g (49.95%)

% Calc: C 61.10, H 5.79, P 10.16, Ag 11.19

% Found: C 60.61, H5.29, P 9.88, Ag 11.33

Melting point: 132-137 ºC

IR (KBr): 3450.30, 3051.37, 2923.89, 2849.61, 1714.34, 1555.08, 1483.28, 1434.92, 1386.65, 1306.68, 1183.53, 1099.85, 1026.14, 998.65, 785.21, 740.09, 719.67, 694.71, 515.19, 481.69, 440.32 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, acetone, chloroform and DMSO

**E.7.9 $[Ag_2(udda)(dppm)_4]$ (47)**

0.432 g (1.0 mmol) of $[Ag_2(udda)]$ in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.730 g (60.83%)

% Calc: C 61.48, H 5.73, P 10.07, Ag 17.53

% Found: C 60.84, H 5.15, P 10.46, Ag 17.98

Melting point: 133-138 ºC

IR (KBr): 3431.91, 3050.22, 2922.36, 2850.19, 1552.42, 1483.32, 1435.08, 1394.67, 1099.33, 999.03, 788.47, 739.67, 721.42, 693.37, 515.21, 480.47, 442.86 $cm^{-1}$.

Solubility: Insoluble in water, partially soluble in methanol, ethanol, DMSO, Chloroform and acetone.

**E.7.10 $[Ag_2(ddda)(dppm)_4].H_2O$ (48)**

0.446 g (1.0 mmol) of $[Ag_2(ddda)]$ in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.7163 g (59.03%)

% Calc: C 61.57, H 6.32, P 9.48, Ag 17.08

% Found: C 61.43, H 5.61, P 9.36, Ag 17.69

Melting point: 126-131 ºC

IR (KBr): 3431.61, 3051.65, 2923.27, 2850.51, 2359.66, 1553.15, 1484.55, 1435.63, 1386.15, 1100.18, 999.41, 789.90, 740.27, 722.98, 694.61, 516.62, 481.04 $cm^{-1}$.

Solubility: insoluble in water, ethanol, acetone, partially soluble in methanol, chloroform, DMSO

**E.7.11 [$Ag_2$(uddca)(dppm)$_4$].2$H_2O$ (49)**

0.460 g (1.0 mmol) of [$Ag_2$(uddca)] in 30 mls of toluene reacted with 0.768 g (2.0 mmol) of dppm.

Yield: 0.8652 g (70.45%)

% Calc: C 60.29, H 6.07, P 9.57, Ag 16.66

% Found: C 59.71, H 5.25, P 9.93, Ag 16.98

Melting point: 127-132 ºC

IR (KBr): 3423.18, 3051.30, 3019.92, 2920.52, 2850.36, 1550.73, 1484.47, 1466.33, 1435.47, 1396.68, 1309.65, 1145.59, 1099.88, 1026.29, 999.31, 788.47, 740.26, 723.32, 693.96, 668.79, 516.56, 479.79, 438.99 $cm^{-1}$.

Solubility: insoluble in water, partially soluble in methanol, ethanol, acetone, chloroform and DMSO

## E.8 SYNTHESIS OF SILVERDICARBOXYLATE DIPHENYLPHOSPHINETHANE COMPLEXES

**E.8.1 [$Ag_2$(prda)(dppe)$_4$].$H_2O$ (50)**

0.319 g (1.0 mmol) of [$Ag_2$(prda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.906 g (81.18%)

% Calc: C 59.41, H 5.41, P 10.39, Ag 18.09

% Found: C 58.24, H 4.48, P 11.32, Ag 18.81

Melting point: 128-133 ºC

IR (KBr): 3431.68, 3051.61, 1556.21, 1482.77, 1434.60, 1331.95, 1175.42, 1100.34, 1026.57, 998.93, 926.06, 742.99, 723.86, 694.59, 654.76, 509.74, 482.64, 447.22 $cm^{-1}$.

Solubility: partially soluble in ethanol, DMSO, insoluble in methanol, acetone, chloroform, water

**E.8.2 [$Ag_2$(bda)(dppe)$_4$] (51)**

0.334 g (1.0 mmol) of [$Ag_2$(bda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.608 g (53.75%)

% Calc: C 60.62, H 5.43, P 10.42, Ag 18.15

% Found: C 59.63, H 4.75, P 10.98, Ag 18.93

Melting point: 129-134ºC

IR (KBr): 3432.01, 3052.01, 1552.07, 1482.66, 1434.25, 1405.33, 1176.51, 1100.09, 1026.42, 998.84, 744.04, 729.65, 694.70, 656.18, 511.84, 479.87 $cm^{-1}$.

Solubility: partially soluble in water, acetone, methanol, ethanol, chloroform and DMSO

**E.8.3 $[Ag_2(pda)(dppe)_3].4H_2O$ (52)**

0.348 g (1.0 mmol) of $[Ag_2(pda)]$ in 30 mls of toluene reacted with 0.797g (2.0 mmol) of dppe.

Yield: 0.7261 g (63.41%)

% Calc: C 53.22, H 5.61, P 8.76, Ag 20.34

% Found: C 52.17, H 4.21, P 9.46, Ag 20.49

Melting point: 130-135ºC

IR (KBr): 3418.67, 3050.54, 1552.60, 1482.99, 1434.13, 1400.26, 1311.86, 1176.71, 1099.57, 1069.05, 1026.53, 998.82, 884.74, 740.81, 726.81, 694.68, 511.33, 481.78, 449.11 $cm^{-1}$.

Solubility: partially soluble in methanol, chloroform, insoluble in ethanol, acetone, DMSO

**E.8.4 $[Ag_2(hxda)(dppe)_4]$ (53)**

0.362 g (1.0 mmol) of $[Ag_2(hxda)]$ in 30 mls of Toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.8416 g (72.56%)

% Calc: C 61.20, H 5.63, P 10.18, Ag 17.73

% Found: C 61.78, H 5.10, P 10.53, Ag 17.11

Melting point: 131-136 ºC

IR (KBr): 3432.85, 3049.13, 2919.94, 1691.01, 1555.63, 1483.18, 1434.45, 1403.85, 1310.76, 1239.33, 1099.39, 1069.60, 1026.86, 999.63, 881.40, 741.52, 718.84, 692.97, 513.53, 482.10 $cm^{-1}$.

Solubility: partially soluble in water, methanol, ethanol, DMSO, insoluble in acetone, chloroform.

**E.8.5 [$Ag_2$(hpda)$(dppe)_3$] (54)**

0.376 g (1.0 mmol) of [$Ag_2$(hpda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.6965 g (59.37%)

% Calc: C 57.89, H 5.45, P 9.14, Ag 21.22

% Found: C 56.84, H 4.80, P 10.26, Ag 21.99

Melting point: 132-137 ºC

IR (KBr): 3427.21, 3049.98, 2927.69, 1548.43, 1482.84, 1434.58, 1401.36, 1308.83, 1177.74, 1100.15, 1069.08, 1026.16, 998.58, 925.59, 743.48, 758.43, 693.36, 509.87, 480.28, 447.93 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, acetone, chloroform and DMSO

**E.8.6 [$Ag_2$(oda)$(dppe)_4$] (55)**

0.390 g (1.0 mmol) of [$Ag_2$(oda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.845 g (71.18%)

% Calc: C 61.75, H 5.83, P 9.95, Ag 17.73

% Found: C 60.13, H 5.02, P 10.25, Ag 17.86

Melting point: 133-138 ºC

IR (KBr): 3441.09, 2935.88, 1545.08, 1483.44, 1434.23, 1398.45, 1175.72, 1100.11, 1027.33, 740.83, 726.94, 693.94, 511.59, 477.76 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, acetone, chloroform and DMSO

**E.8.7 [$Ag_2$(nda)$(dppe)_4$].$2H_2O$ (56)**

0.404 g (1.0 mmol) of [$Ag_2$(nda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.7634 g (63.56%)

% Calc: C 60.29, H 6.07, P 9.57, Ag 16.66

% Found: C 60.43, H 5.17, P 10.71, Ag 16.88

Melting point: 127-132ºC

IR (KBr): 3433.58, 3050.30, 2922.85, 1560.67, 1482.99, 1434.25, 1399.80, 1175.42, 1099.22, 1026.42, 999.34, 741.71, 723.43, 694.82, 510.84,481.90 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, acetone, chloroform and DMSO.

**E.8.8 $[Ag_2(dda)(dppe)_4]$ (57)**

0.418 g (1.0 mmol) of $[Ag_2(dda)]$ in 30 mls of toluene reacted with 0.797 (2.0 mmol) of dppe.

Yield: 0.8132 g (66.93%)

% Calc: C 62.27, H 6.02, P 9.73, Ag 16.95

% Found: C 62.52, H 5.57, P 10.29, Ag 16.17

Melting point: 128-133ºC

IR (KBr): 3438.20, 3051.81, 2923.91, 2850.61, 1556.19, 1482.94, 1434.57, 1404.53, 1233.75, 1174.62, 1099.92, 1026.53, 999.10, 744.66, 726.85, 694.85, 510.55, 481.80 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, acetone, chloroform, partially soluble in DMSO

**E.8.9 $[Ag_2(udda)(dppe)_4].H_2O$ (58)**

0.432 g (1.0 mmol) of $[Ag_2(udda)]$ in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.950 g (77.29%)

% Calc: C 61.67, H 6.18, P 9.49, Ag 16.53

% Found: C 61.49, H 5.51, P 9.29, Ag 16.13

Melting point: 129-134 ºC

IR (KBr): 3439.42, 3052.04, 2923.37, 2850.50, 1550.42, 1483.01, 1434.50, 1399.88, 1311.59, 1176.36, 1099.98, 1026.51, 999.24, 729.77, 695.28, 509.52, 482.64 $cm^{-1}$.

Solubility: partially soluble in water, DMSO, chloroform, insoluble in methanol, ethanol and acetone.

**E.8.10 [$Ag_2$(ddda)$(dppe)_4$] (59)**

0.446 g (1.0 mmol) of [$Ag_2$(ddda)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.5731 g (46.10%)

% Calc: C 62.78, H 6.20, P 9.52, Ag 16.57

% Found: C 63.62, H 5.74 , P 9.59, Ag 16.61

Melting point: 130-135ºC

IR (KBr): 3442.72, 3052.64, 2920.17, 2849.27, 1697.99, 1637.97, 1555.56, 1482.84, 1434.42, 1403.17, 1255.57, 1185.55, 1099.39, 1026.56, 999.35, 881.87, 743.43, 695.04, 512.03, 481.54 $cm^{-1}$.

Solubility: insoluble in water methanol, ethanol, DMSO, soluble in acetone, chloroform.

**E.8.11 [$Ag_2$(uddca)$(dppe)_4$] (60)**

0.460 g (1.0 mmol) of [$Ag_2$(uddca)] in 30 mls of toluene reacted with 0.797 g (2.0 mmol) of dppe.

Yield: 0.681 g (54.17%)

% Calc: C 63.02, H 6.29, P 9.42, Ag 16.41

% Found: C62.40, H5.66, P 9.89, Ag 16.75

Melting point: 131-136 ºC

IR (KBr): 3439.52, 3051.83, 2922.59, 2850.66, 1741.22, 1630.31, 1551.14, 1483.12, 1466.31, 1434.38, 1400.48, 1310.81, 1274.67, 1175.44, 1099.70, 1069.56, 1026.98, 999.30, 881.77, 743.05, 728.98, 694.95, 510.92, 481.88 $cm^{-1}$.

Solubility: insoluble in water, DMSO, soluble in methanol, ethanol, acetone, chloroform.

## E.9 BIOLOGICAL PREPARATIONS AND METHODS

Fungal isolates: A *Candida albicans* isolate was obtained from ATCC (American Type Culture Collection, Maryland USA) 10231. The isolate was stored on Sabouraud Dextrose Agar (SDA) plates at 4°C, and was sub cultured monthly from the initial culture received.

Sterilisation: was achieved by autoclaving at 121°C and 100 lbs/inch for 15mins.

Cell density: 0.250 OD cells in 5mls of Phosphate Buffered Saline (PBS).

R1 Minimal Media (R1MM): is a media made up of Yeast Nitrogen Base without amino acids (Ynb) obtained from Becton, Dickenson and Company (Ref: 291940) and D (+) Glucose Monohydrate obtained from Reidal-de Haën (Charge lot: 61850). Ynb (0.67g) was dissolved in 100 ml of cold distilled water along with D (+) Glucose Monohydrate (2 g) in a 200 ml duran bottle. The resulting solution was then left to stand for 5 mins and then autoclaved, after autoclaving the bottle was allowed to cool before transfer to multiwell plate. The media was stored at 4°C.
Tests were carried out on overnight cultures of candida grown in sabraud's agar (Oxoid) which was made up according to manufacturing instructions. The antifungal experiments were carried out in R1 minimal media.

Phosphate buffer saline (PBS): was obtained from Sigma (Lot 71K8201) in tablet form and was prepared as follows:
1 tablet was dissolved in cold distilled water (100 ml) and the resulting solution autoclaved for 15 mins.

### E.9.1 Preparation of complex solutions for antimicrobial susceptibility testing

Solutions of suspensions of test complexes were prepared by dissolving (0.1 g) in 5% (5 ml) of DMSO and diluting to 100 $cm^3$ using distilled water to yield a stock solution at a concentration of 1000 μg/ml.

### E.9.2 Antimicrobial Susceptibility testing methods

Yeast susceptibility testing: Each test complex was made into solution following the method, from these stock solutions a series of different concentrations were obtained by dilution. Concentrations of 1.0 μg/ml, 0.5 μg/ml, 0.25 μg/ml, 0.1 μg/ml, 0.09 μg/ml, 0.08 μg/ml, 0.07 μg/ml and 0.05 μg/ml were obtained and through testing the $IC_{50}$ (minimum inhibitory concentration) for each compound was calculated, this was done as follows:

96 well microarray analysis plates (Figure 69*)* were used for yeast susceptibility testing. These plates contained 96 wells in which 10μg/ml of each test solution could be added to every three consecutive wells. A Control, Blank, Amphotericin B (Amp B), Silver Nitrate ($AgNO_3$) and Silver Acetate ($Ag_2(CH_3COO)_2$) were also added to the plate. Before each experiment the candida cell density was determined and adjusted to OD 0.25 by diluting in PBS (Sigma Aldrich), made up according to manufacturer's instructions.

Control 1: This was used as a standard to which the compounds could be tested against. The control was a suspension of R1 minimal media containing 0.250 OD cells of *C. albicans.* 100 μl of the control media was then added to the first three wells on the plate.

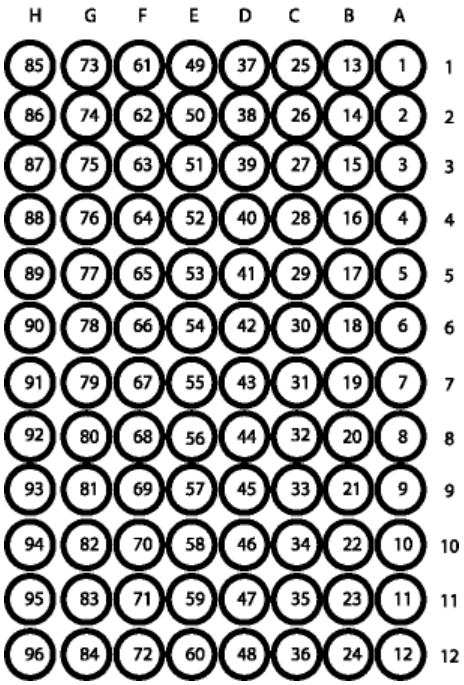
Control 2: Blank; this was a solution of R1MM (100 μg/ml) usually added to the last three wells on the plate, this was a reference to show that the media containing no cells and no test solution would show no growth of cells.

Control 3: Amphotericin B; Amp B is well known antifungal agent. This was added to the cells to see how good the test compounds measured against one of the best on the market. 100 μg/ml of this solution was added to the next three consecutive wells after the control 1.

Control 4: Silver Nitrate ($AgNO_3$) and Silver acetate (AgAoc); were added to see how silver compounds containing no ligand derivative would fair against the test complexes containing a dicarboxylic acid. 10 μg/ml of these solutions were added to the next wells after Amp B. Test complexes were now added at different concentrations to the next available wells.

To the wells containing the test complexes, Amp B, $AgNO_3$ and $Ag_2(CH_3COO)_2$, 90 μg/ml of the R1MM containing *C. albicans* cells were added, the plate was then loaded onto the spectrophotometer and measured at a temp of 37 ºC and left for 24 hrs, with readings being taken every 4 hrs. Each run was done in triplicate meaning it was done once a day for three days. The results were then calculated for $IC_{50}$ of each complex.

***Figure 69***: 96 well plate



### E.9.2.1 Antibacterial test

The antibacterial activity of a series of silver inorganic complexes against a selection of Grampositive and Gramnegative bacteria was determined using inoculated 96 well plates. A total of seven concentrations of each of silver complex, ligand and silver nitrate control were assessed for antibacterial activity. These concentrations were: 50 ppm, 25 ppm, 10 ppm, 5 ppm, 2.5 ppm, 1 ppm and 0.1 ppm. The water insoluble complexes were initially dissolved in DMSO, and subsequently diluted in de-ionised water to give the desired concentrations. The bacterial strains tested were MRSA (clinical isolate), *S. aureus* (ATCC 25922), *E. coli* (ATCC 25923) and *E. coli* (clinical isolate). Stock cultures of the bacteria were grown on plate count agar (PCA-3% w/v tryptone, 1% w/v glucose, 2.5 % w/v yeast, 9 % w/v agar, Oxoid). These organisms were grown overnight in nutrient rich broth to give a concentration of approximately $10^8$ cfu/ml. These were diluted one in ten thousand with maximum recovery diluent (MRD – 1 % w/v peptone, 8.5 % w/v NaCl, Oxoid) to give working concentrations of approximately $10^4$ cfu/ml. 10 μl aliquots of each concentration of material was placed in separate wells of a 96 well plate. Each test well was inoculated with 90 μl of the working $10^4$ cfu/ml bacterial isolates. The resulting wells were incubated overnight at 37°C. Wells containing the ligands, silver nitrate (reference) and bacterial blanks were also prepared. All tests were performed in duplicate. The optical absorbance of the wells was obtained using an ELISA reader at 632 nm. The resulting absorbance values were plotted against the concentration.

# CONCLUSION

The purpose of this study was to generate a series of light stable silver complexes for application as potential antimicrobial agents. The strategy employed the use of the aliphatic α, ω-dicarboxylic acids HOOC-$(CH_2)_n$-COOH (where n = 1-11) as primary ligands and counter ions. These versatile ligands have previously been shown, in this laboratory, to promote variations in structure and nuclearity (chain length dependent). The auxiliary ligands chosen were the neutral donor phosphines $PPh_3$, dppm and dppe which are known to stabilize $Ag^+$ complexes.[66]

The α, ω-dicarboxylic acids reacted smoothly with [$Ag(CH_3COO)$] to yield the silver dicarboxylate complexes [$Ag_2$(prda)] **(1)**, [$Ag_2$(bda)] **(2)**, [$Ag_2$(pda)] **(3)**, [$Ag_2$(hxda)] **(4)**, [$Ag_2$(hpda)]**(5)**, [$Ag_2$(oda)] **(6)**, [$Ag_2$(nda)] **(7)**, [$Ag_2$(dda)] **(8)**, [$Ag_2$(udda)] **(9)**, [$Ag_2$(ddda)] **(10)** and [$Ag_2$(uddca)] **(11)**. Complexes **1-11** were reacted with $PPh_3$ in 1:2.5, 1:4 and 1:6 molar ratios and with the dppm and dppe in 1:2 molar ratios, respectively.

Thecomplexes[$Ag_2$(prda)($PPh_3$)$_3$](**12**),[$Ag_2$(bda)($PPh_3$)$_3$].$C_7H_8$(**13**), [$Ag_2$(pda)($PPh_3$)$_3$].2$H_2O$ (**14**), [Ag(hxdaH)($PPh_3$)$_2$] (**15**) {Ag(hpdaH)($PPh_3$)$_3$.2$H_2O$}$_n$(**16**),{$Ag_2$(oda)($PPh_3$)$_3$.2$H_2O$}$_n$(**17**), [Ag(ndaH)($PPh_3$)$_2$](**18**), [$Ag_2$(dda)($PPh_3$)$_4$].2$C_7H_8$(**19**), [$Ag_2$(udda)($PPh_3$)$_2$] (**20**), [Ag(ddda)($PPh_3$)$_3$] (**21**) and [Ag(uddcaH)($PPh_3$)$_2$] (**22**) resulted from the reaction of the relevant Ag(I) dicarboxylate salt with 2.5 equivalents of $PPh_3$.

The complexes [$Ag_2$(prda)($PPh_3$)$_3$].$H_2O$ (**23**), [$Ag_2$(bda)($PPh_3$)$_4$] (**24**), [$Ag_2$(pda)($PPh_3$)$_4$] (**25**), [Ag(hxda)($PPh_3$)$_4$] .2$H_2O$(**26**), [$Ag_2$(hpda)($PPh_3$)$_4$].$C_7H_8$(**27**), [$Ag_2$(oda)($PPh_3$)$_4$].2.$C_7H_8$(**28**), [$Ag_2$(oda)($PPh_3$)$_4$] (**28A**), [$Ag_2$(ndaH)($PPh_3$)$_4$].2$H_2O$ (**29**), [$Ag_2$(dda)($PPh_3$)$_4$].$H_2O$ (**30**), [$Ag_2$ (udda) ($PPh_3$)$_3$] (**31**), [$Ag_2$ (udda) ($PPh_3$)$_4$](**31A**), [Ag(ddda)($PPh_3$)$_3$]$_n$ **(32)** and [Ag($PPh_3$)$_2$(HOOC$(CH_2)_9$COO)]**(33)** resulted from the reaction of the relevant Ag(I)dicarboxylate salt with 4 equivalents of $PPh_3$.

Attempts to react complexes **1-11** with $PPh_3$ in a 1:6 ratio yielded the same product as obtained when 4 equivalent of $PPh_3$ were employed and where the dicarboxylate ligands were propanedioate (prda), butanedioate (bda), pentanedioate (pda), nonanedioate (nda) and decanedioate (dda). The complexes [Ag(hxdaH)($PPh_3$)$_3$].$C_7H_8$

(**34**), $[Ag_2(hpda)(PPh_3)_5].C_7H_8$ (**35**) $[Ag_2(oda)(PPh_3)_5].2C_7H_8$ **(36)** $[Ag_2(udda)(PPh_3)_4]$ **(37)**, $[Ag_2(uddca)(PPh_3)_5]$ **(38)**, $[Ag_2(uddca)(PPh_3)_6]$ **(38A)** were successfully generated.

Complexes **1-11** were reacted with dppm in a 1:2 molar ratio to yield the complexes $[Ag_2(prda)(dppm)_3]C_7H_8$ **(39),** $[Ag_2(bda)(dppm)_3].C_7H_8$ (**40**), $[Ag_2(pda)(dppm)_4]$ (**41**), $[Ag_2(hxda)(dppm)_4]$ (**42**), $[Ag_2(hpda)(dppm)_4]$ (**43**), $[Ag_2(oda)(dppm)_4]$ **(44)**, $[Ag_2(nda)(dppm)_4]$ **(45),** $[Ag(ddaH)(dppm)_3].3H_2O$ **(46),** $[Ag_2(udda)(dppm)_4]$ **(47)**, $[Ag_2(ddda)(dppm)_4].H_2O$ **(48)**, $[Ag_2(uddca)(dppm)_4].2H_2O$ **(49)**, $[Ag_2(dppm)_2(OAc)_2].3C_7H_8$ **(49A).**

Complexes **1-11** were reacted with dppe in a 1:2 molar ratio using the same procedure employed for the dppm reactions to yield the complexes $[Ag_2(prda)(dppe)_4].H_2O$(**50**), $[Ag_2(bda)(dppe)_4]$(**51**), $[Ag_2(pda)(dppe)_3].4H_2O$(**52**), $[Ag_2(hxda)(dppe)_4]$(**53**), $[Ag_2(hpda)(dppe)_3]$(**54**), $[Ag_2(oda)(dppe)_4]$(**55**), $[Ag_2(nda)(dppe)_4].2H_2O$ (**56**), $[Ag_2(dda)(dppe)_4]$ (**57**), $[Ag_2(udda)(dppe)_4].H2O$ (**58**), $[Ag_2(ddda)(dppe)4]$ (**59**), $[Ag_2(uddca)(dppe)_4]$ (**60**).

All 60 complexes were found to have limited solubilities and complexes **12-60** were all relatively light stable compared to simple silver salts such as $AgNO_3$ and their structures were found to be diverse (the structures of complexes **16, 17, 18, 22, 28, 31A, 32, 33, 38A** and **48A** were determined by X-ray crystallography) with mononuclear, dinuclear, polynuclear and polymeric species generated.

The antimicrobial experiments have shown that all of the metal free dicarboxylic acids and phosphine based ligands are relatively poor antifungals and display no antibacterial activity. Complexes **1-11** are potent in-vitro anti-*Candida* agents which display activity superior/comparable to the clinically used $AgNO_3$ and the state-of -the -art organic drug Amphothericin B. Only five of the silver dicarboxylates (complexes **1, 4, 5, 6** and **7**) displayed good antibacterial activity, although it was significantly less than that of $AgNO_3$. Furthermore, unlike the the activity of $AgNO_3$ these five complexes displayed some discrimination in activity towards the Gram positive (*S. aureus* /MRSA) and Gramnegative (*E.coli*) bacteria. Therefore, it is

suggested that the silver dicarboxylate complexes **1-11** do not act on microbial cells in the same way as $AgNO_3$.

All 27 of the $PPh_3$ complexes (**12-38**) exhibited significant antifungal activity against the *Candida albicans* cells although their activity is, on average, over ten times less than that of the equivalent silver dicarboxylate. Only complexes **14, 31, 33, 37** and **38** are active against the bacterial cells tested. Complexes **31, 37** and **38** are the only complexes that display higher antibacterial activity (comparable to that of $AgNO_3$) than antifungal activity, a trend not previously observed. Complexes **31, 37** and **38** represent potential therapeutics that warrent further investigation as novel antibacterial agents.

The dppm and dppe derivatives **39-60** all exhibited significant antifungal activity against the *Candida albicans* cells. However, with the exception of complex **39,** most of their activities are again significantly less than that of the equivalent silver dicarboxylate. Only complexes **39, 41** and **52** display any activity against the bacterial cells tested. Complex **41** is interesting as it exhibits good activity against the Gram positive MRSA but it is inactive agaist the Gramnegative *E.coli.* Complexes **39** and **52** display some discrimination in activity towards the Grampositive (MRSA) and Gramnegative (*E.coli*) bacteria.

In conclusion this research has shown that structurally diverse, light stable silver complexes can be synthesised easily using the aliphatic α, ω-dicarboxylic acids as primary, and phosphines as stabilizing donor, ligands. All of the sixty complexes generated are effective antifungal agents with a variation in the degree of activity reflecting their structural diversity. This variation in antifungal activity and the fact that only 13 of the complexes display antibacterial properties suggests that a mode of action other than simple silver ion release may be responsible for their antimicrobial properties. This class of complex represents a very interesting group of potential antifungal agents and a number of the complexes (particularly **31, 37** and **38**) may offer significant potential as broad spectrum therapeutic antibacterial drugs.

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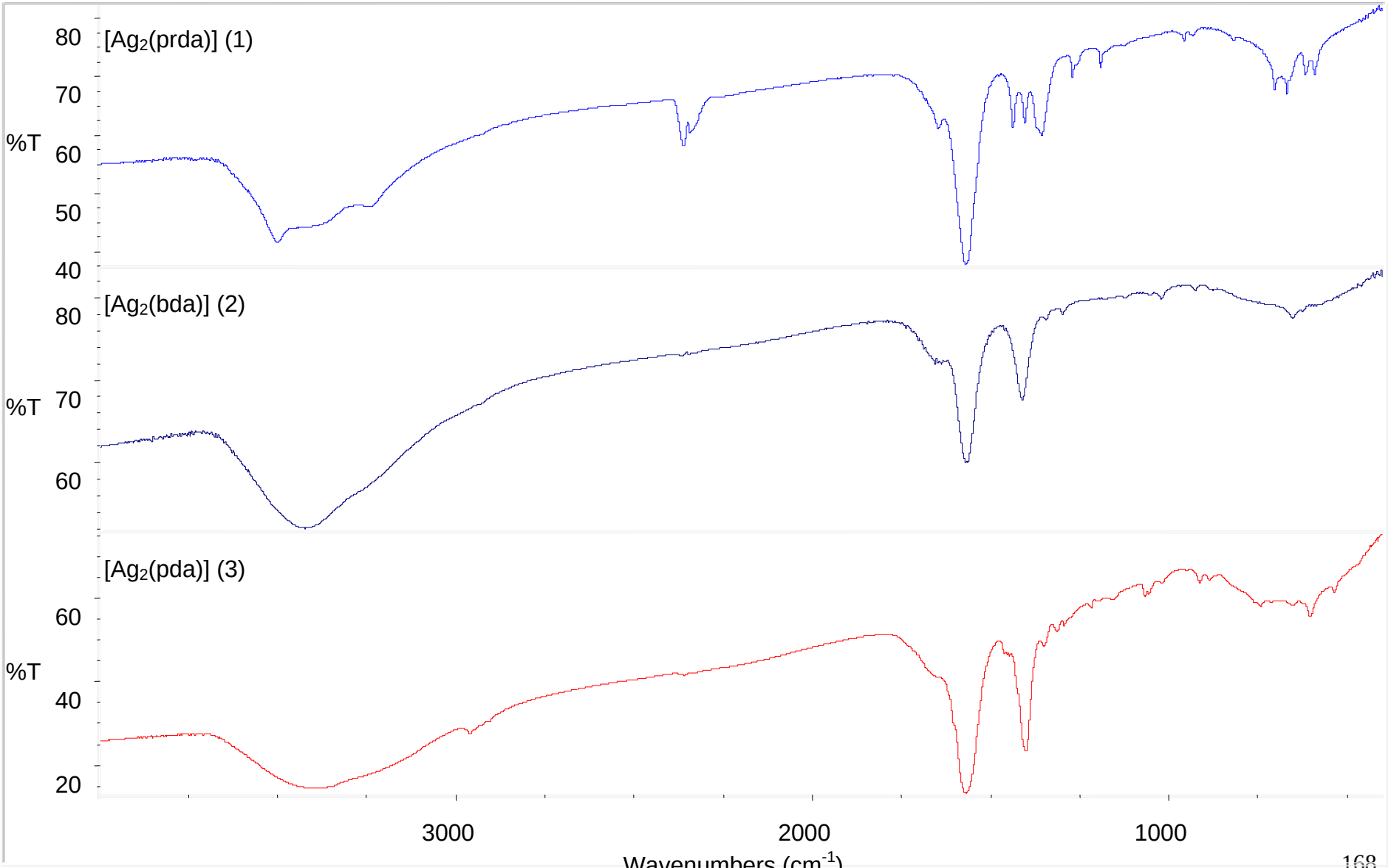
# APPENDIX 1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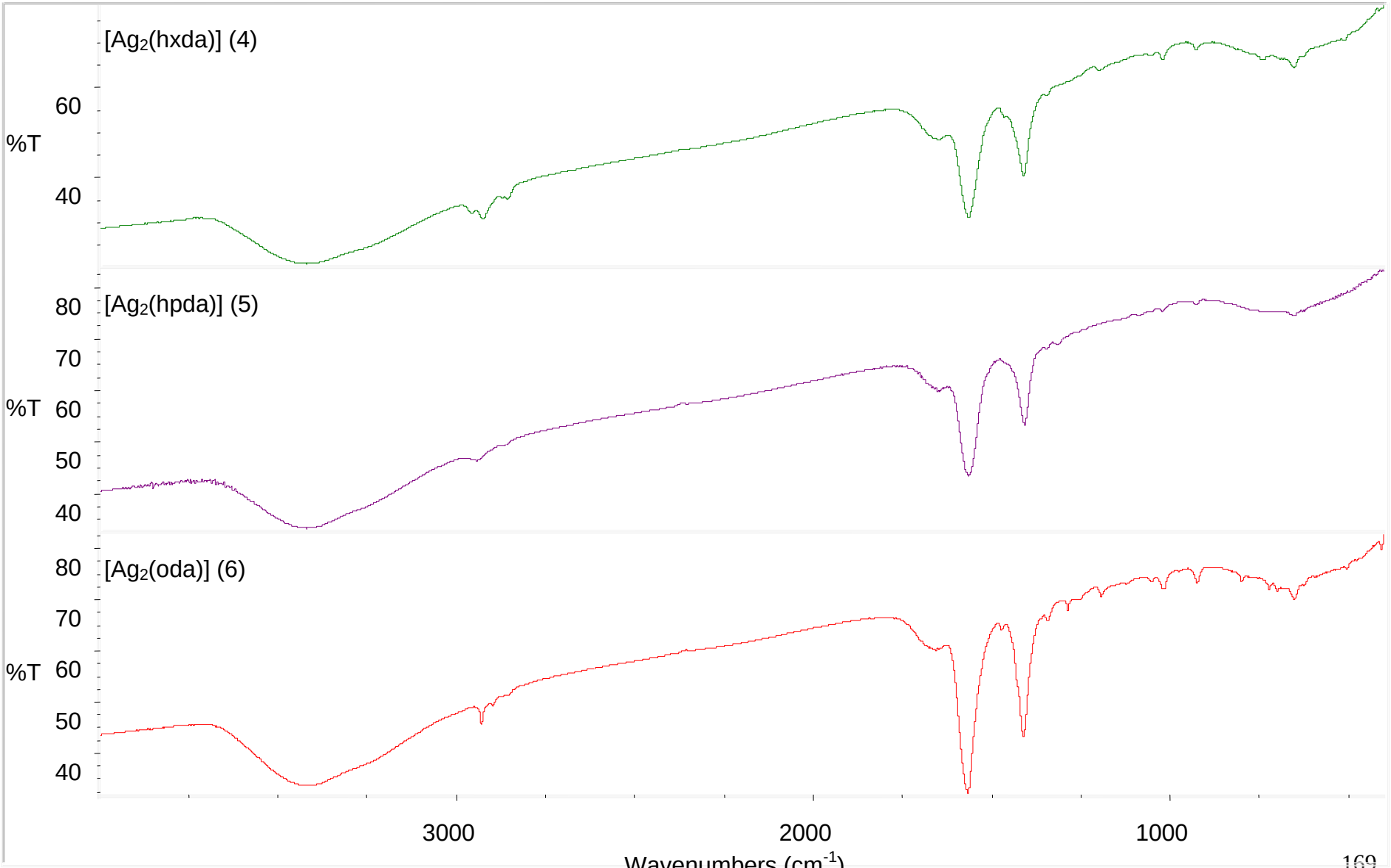
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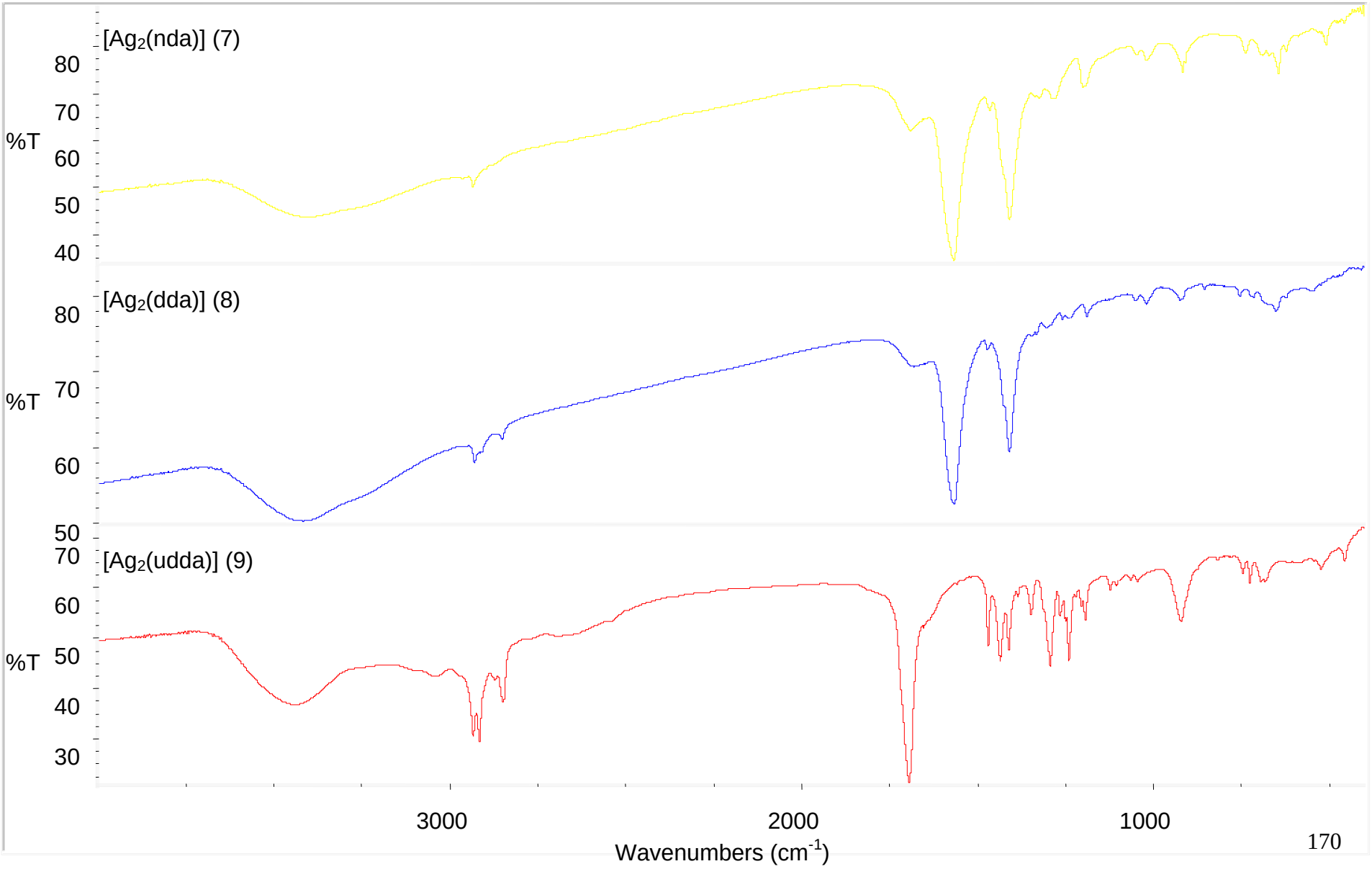
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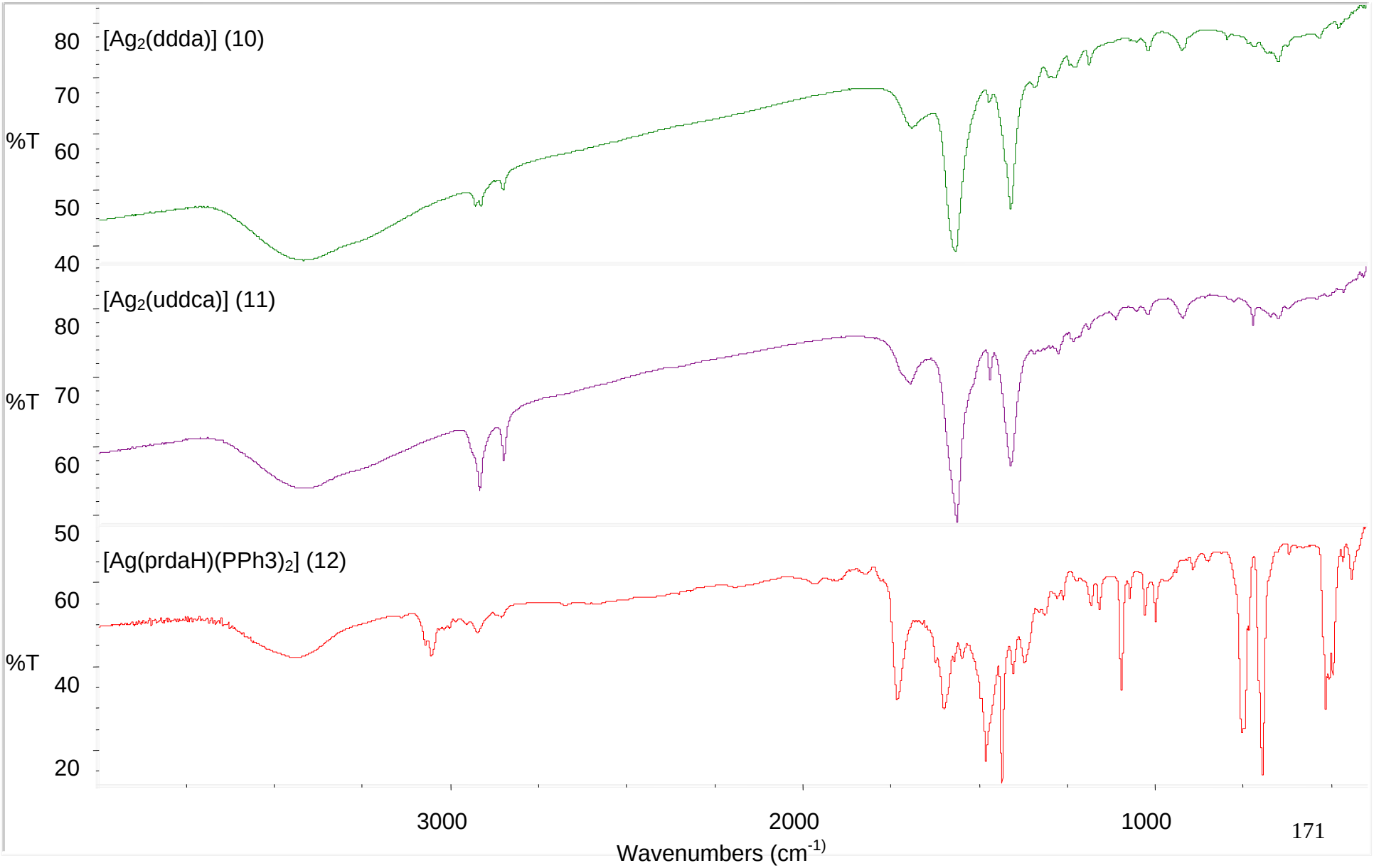
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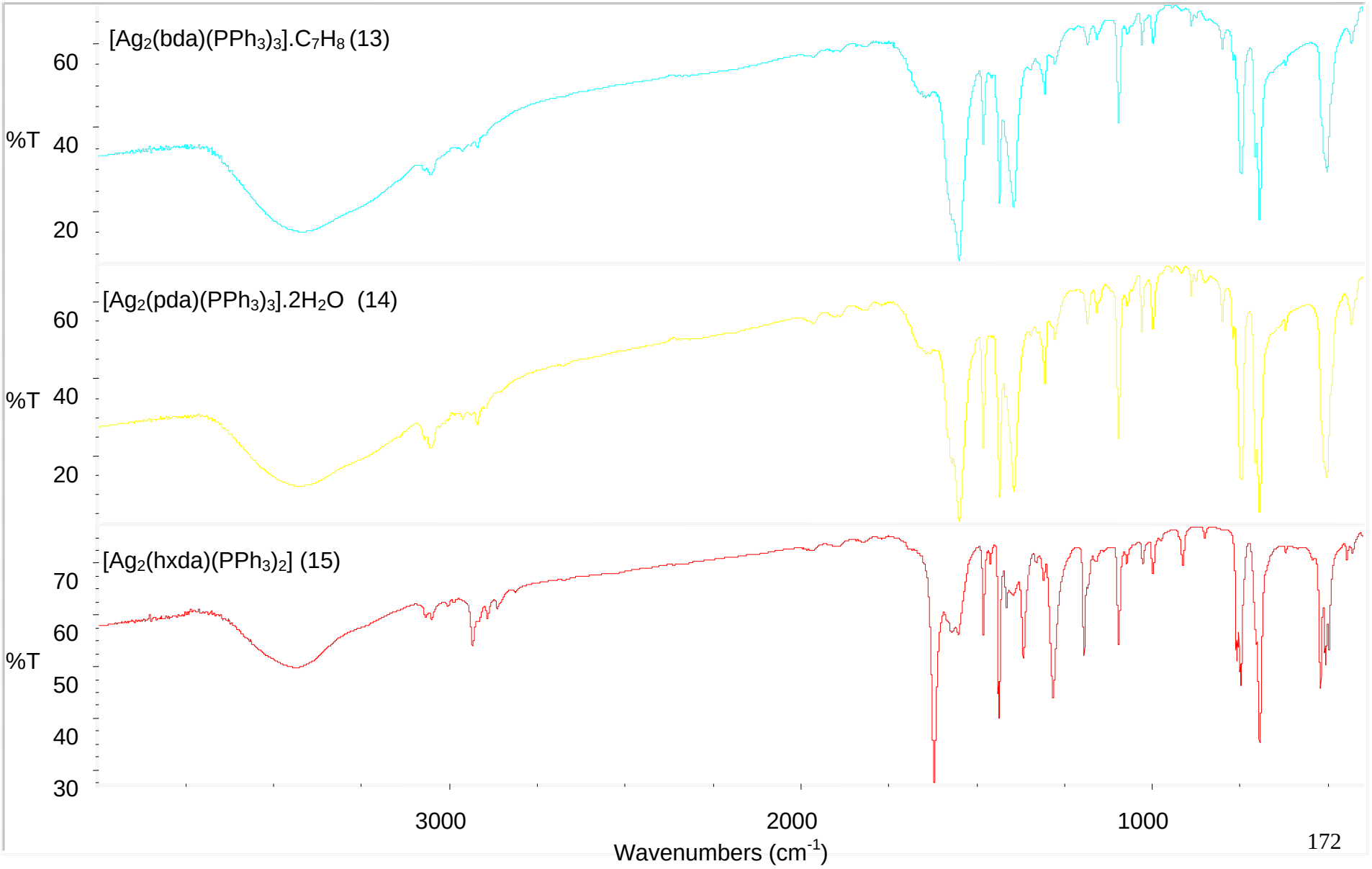
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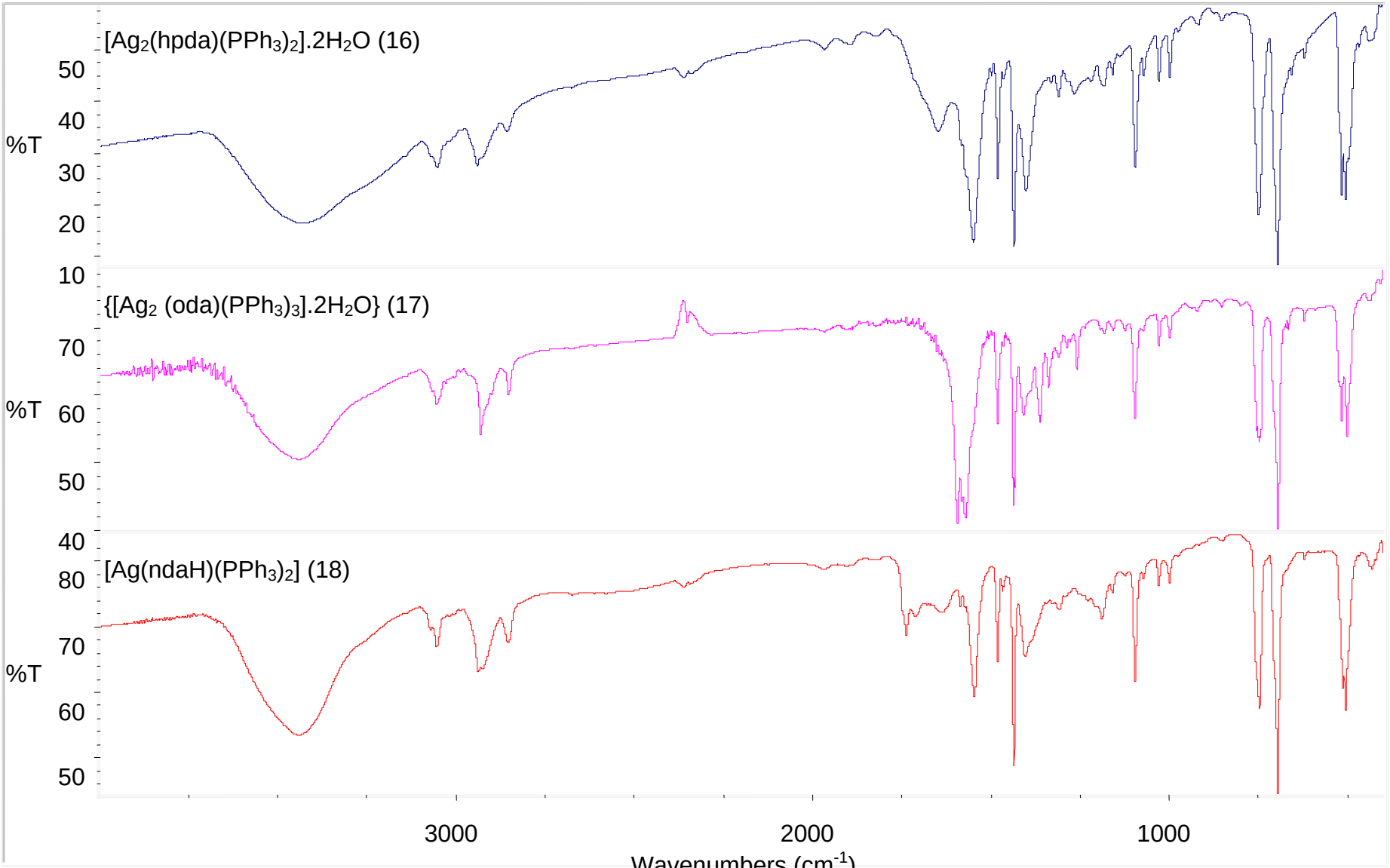
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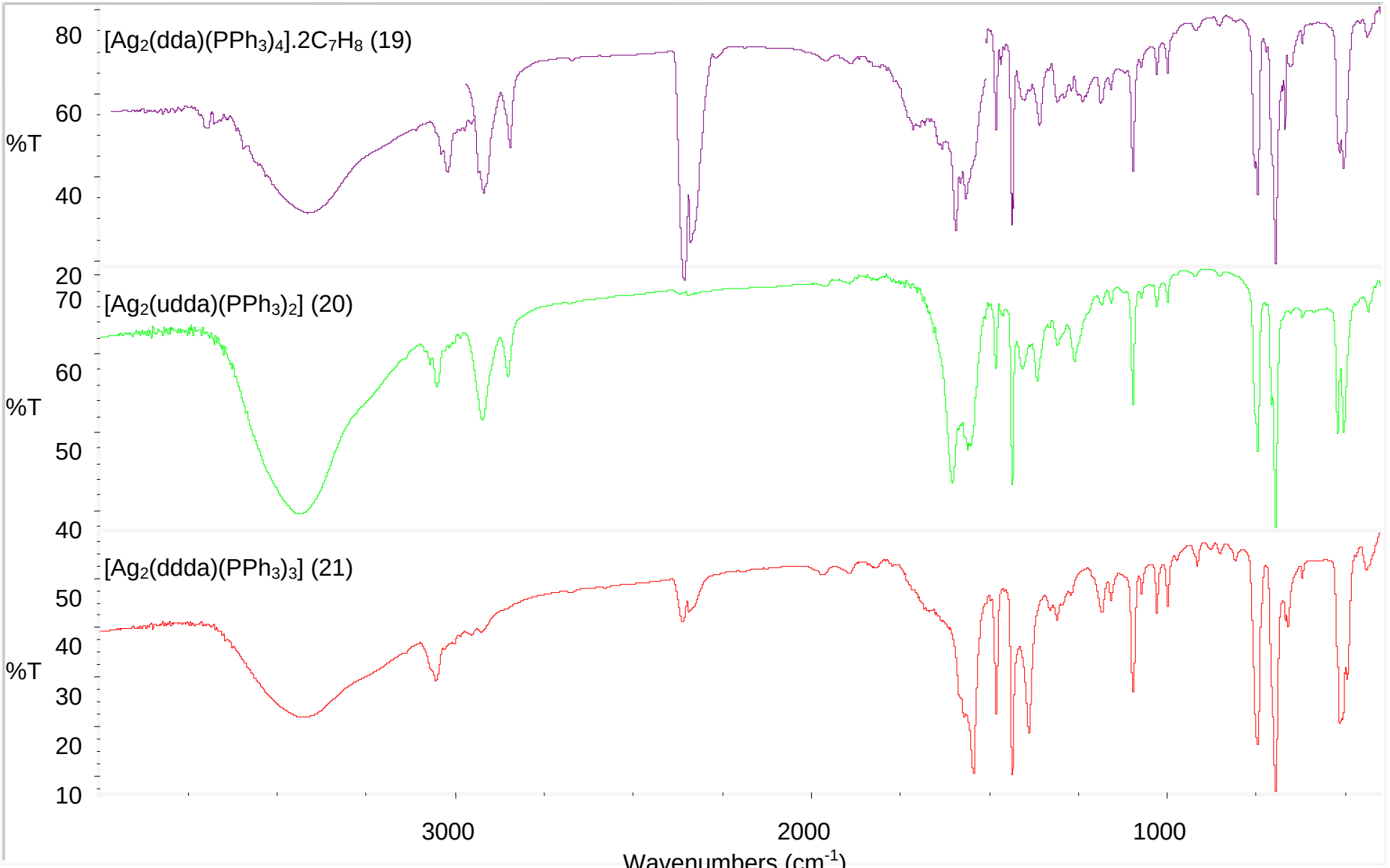
Wavenumbers (cm-1)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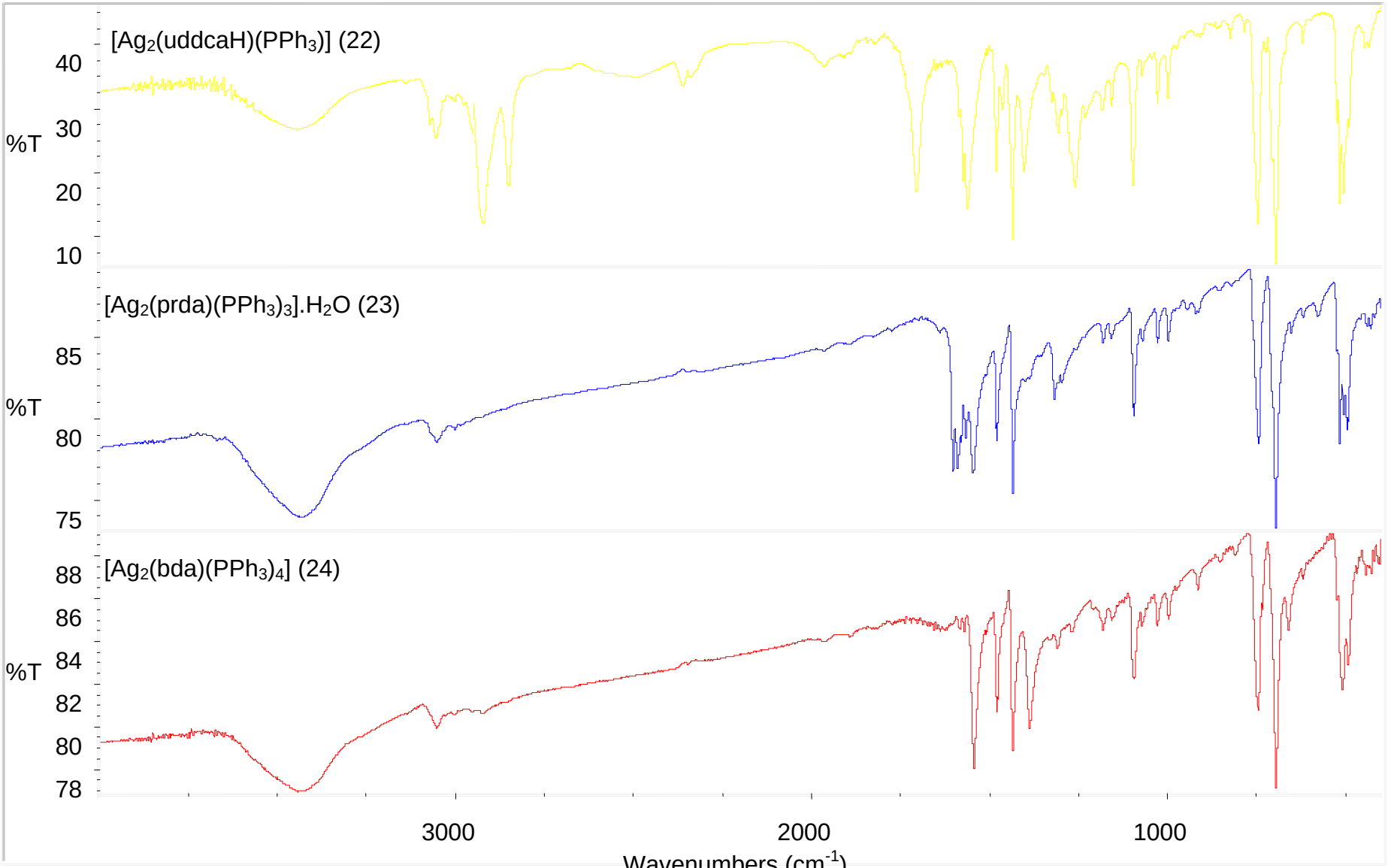
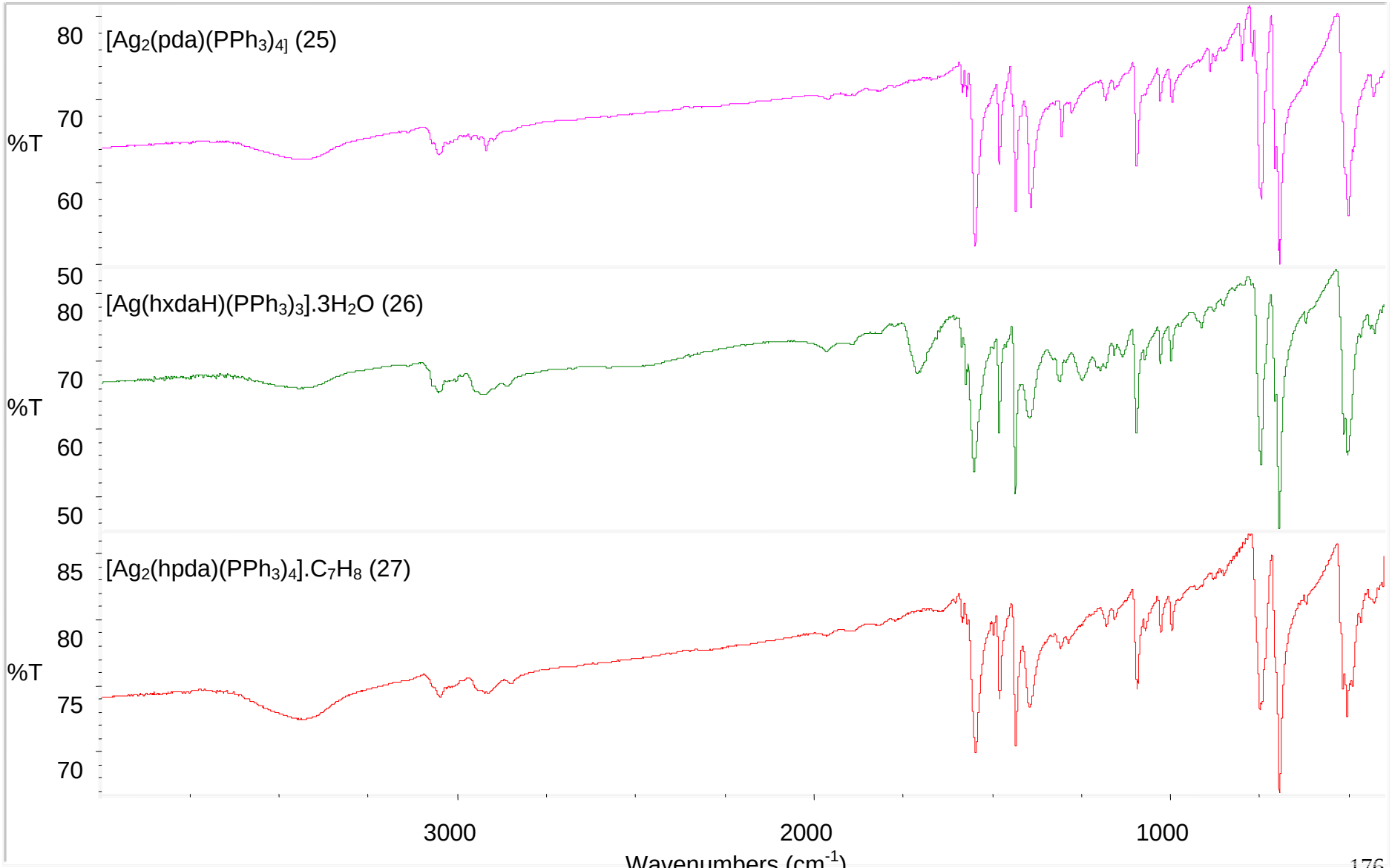
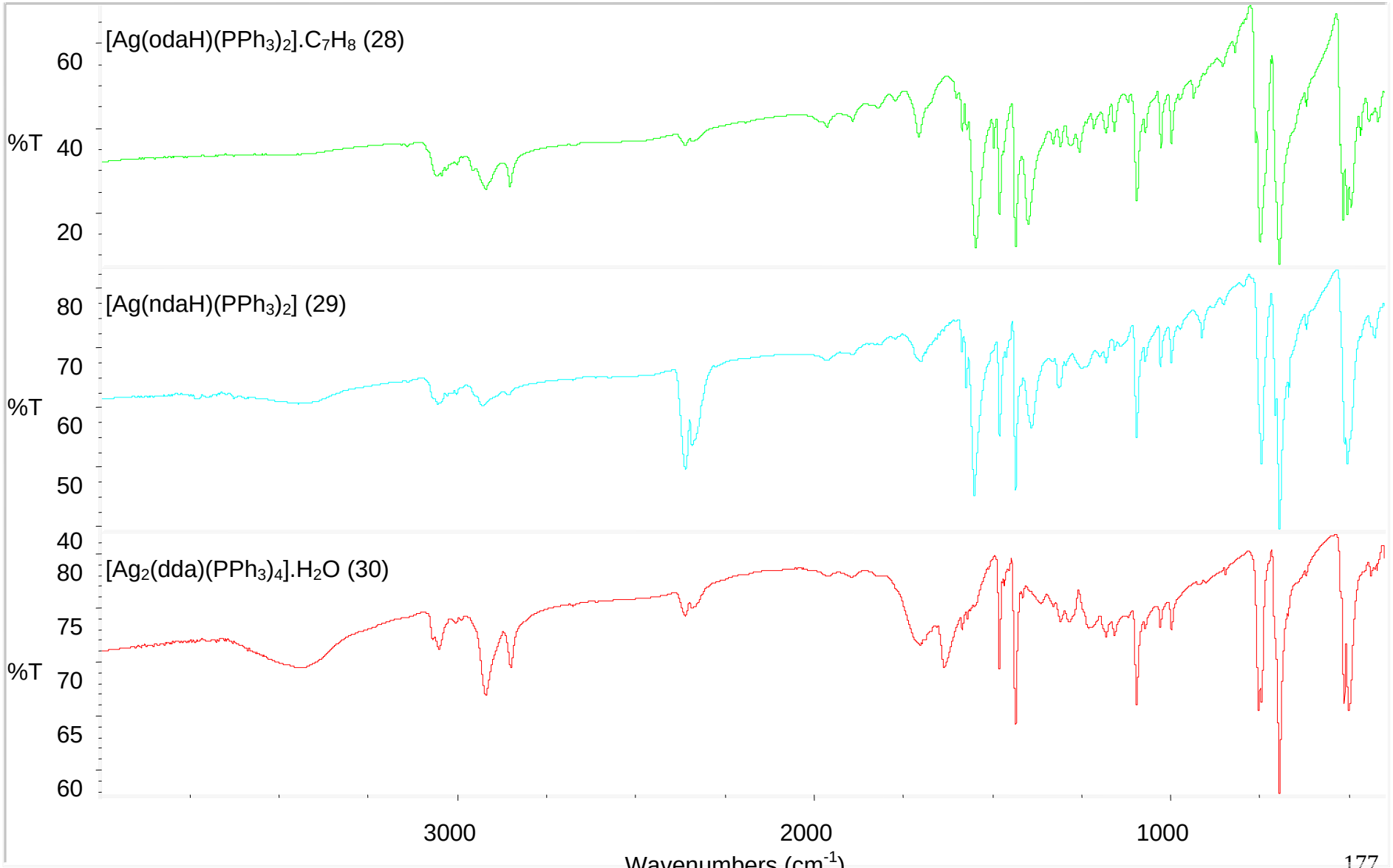
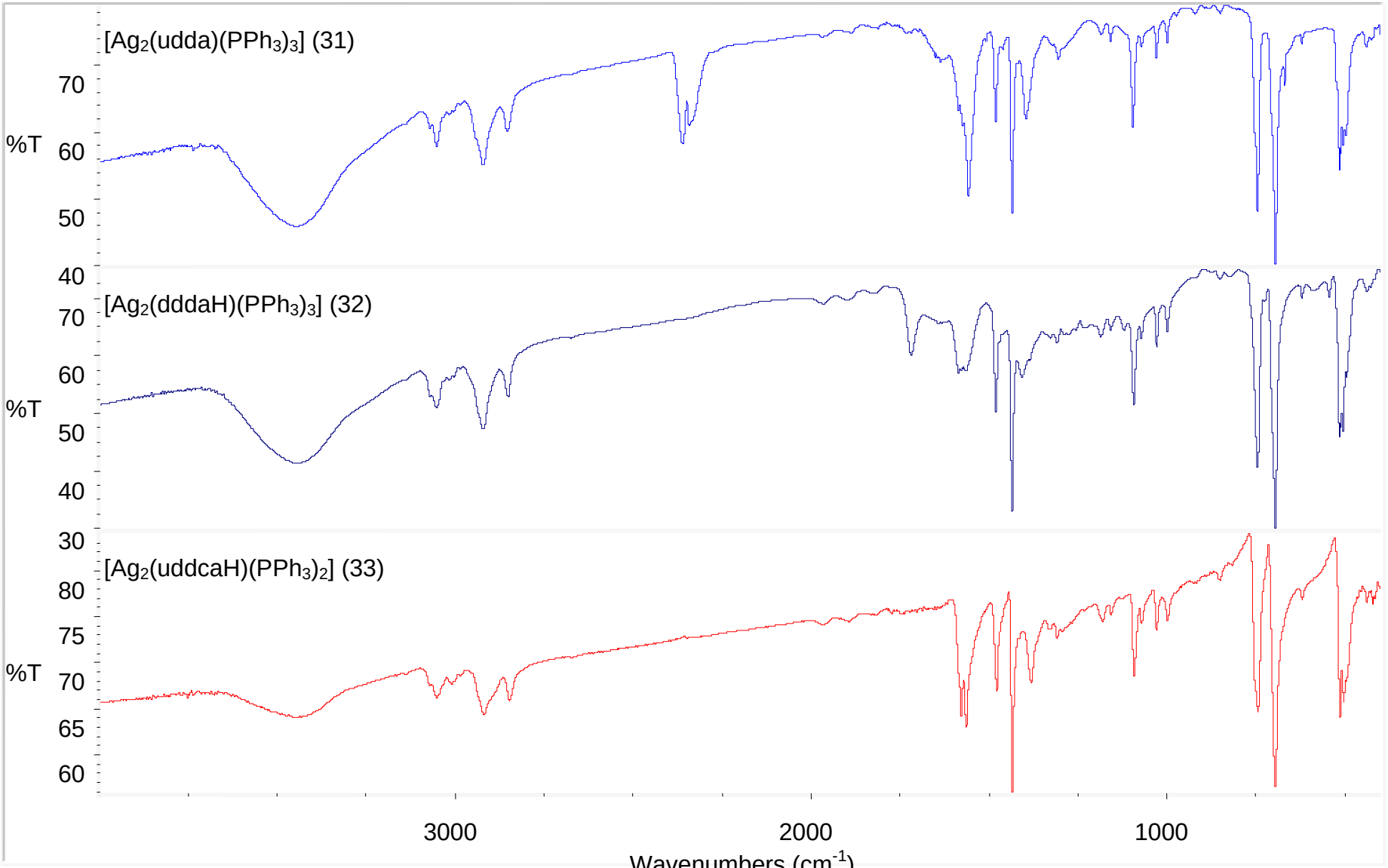
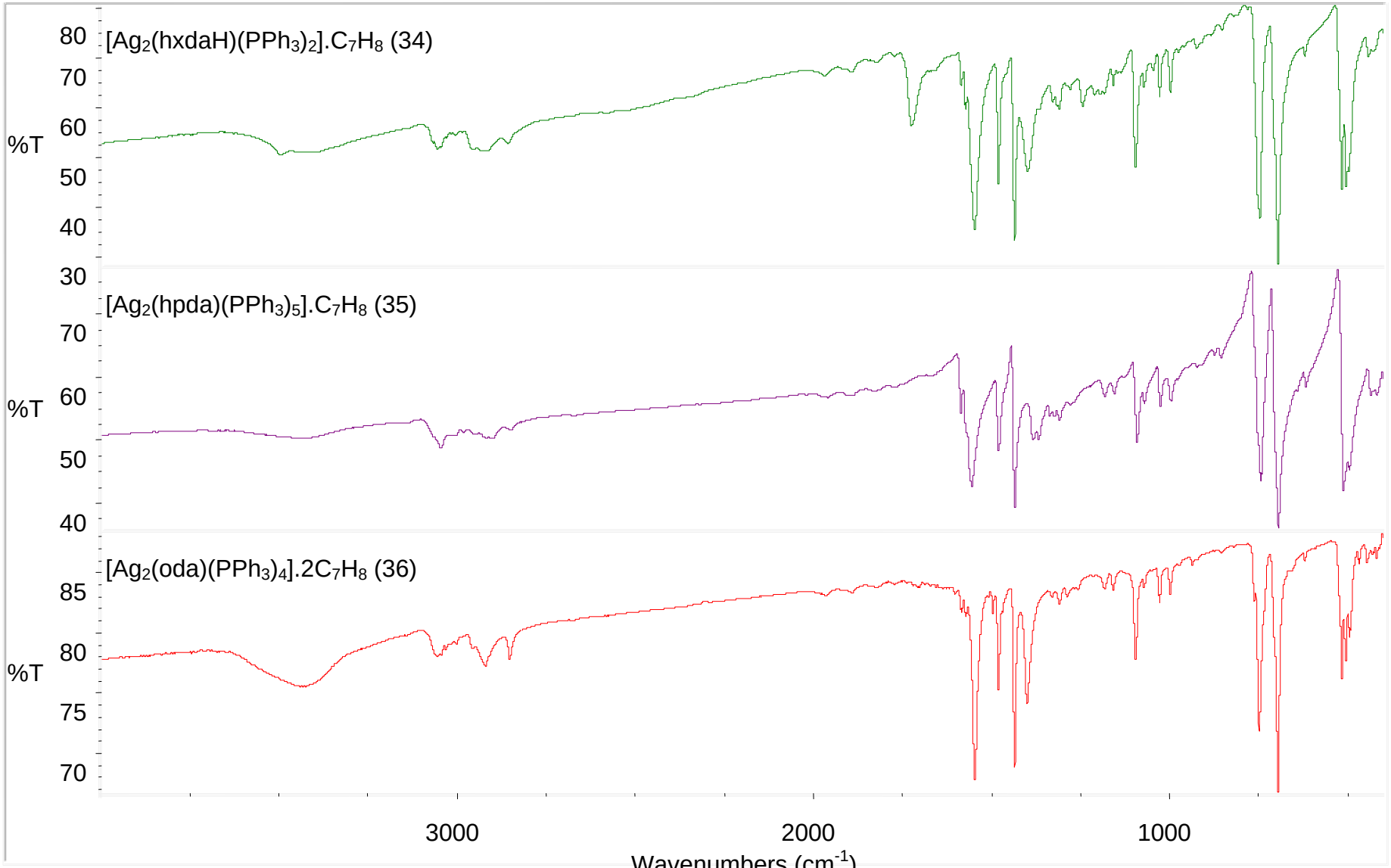
30
20
10
3000
2000
1000
Wavenumbers (cm-1)

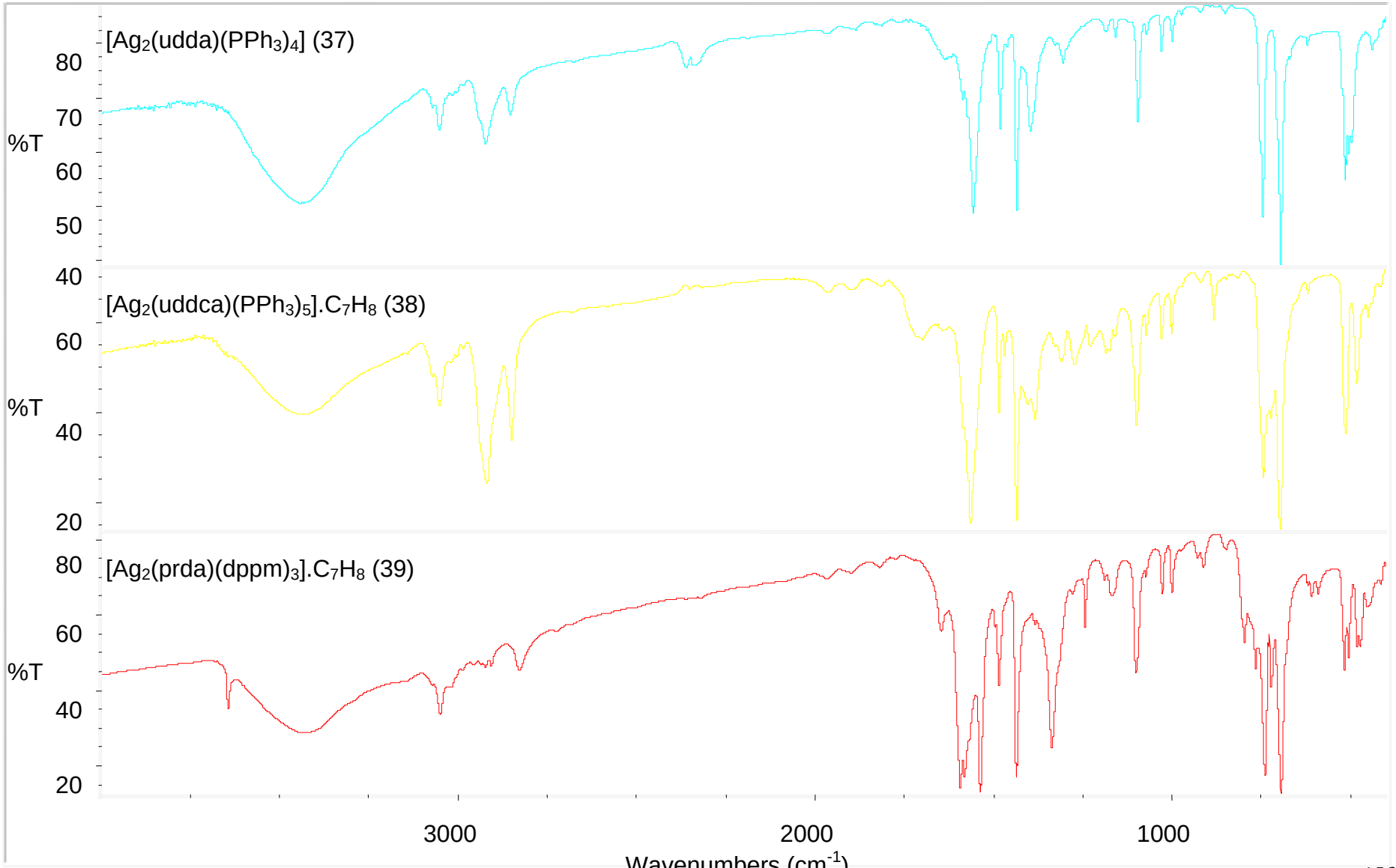

[Ag2(uddcaH)(PPh3)] (22)
%T
40
30
20
10
[Ag2(prda)(PPh3)3].H2O (23)
%T
85
80
75
[Ag2(bda)(PPh3)4] (24)
%T
88
86
84
82
80
78
3000
2000
1000
Wavenumbers (cm-1)

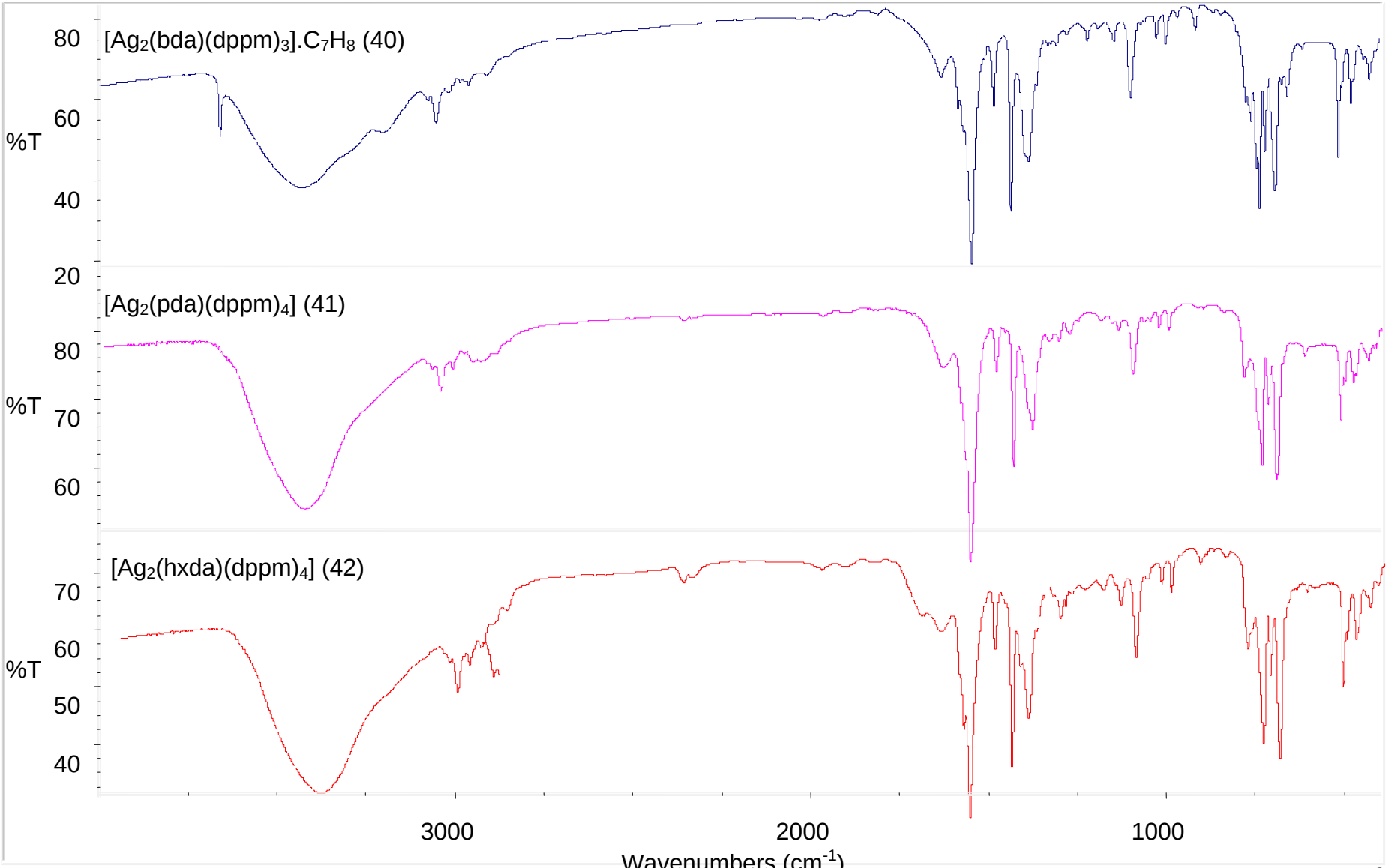

[Ag2(pda)(PPh3)4] (25)
[Ag(hxdaH)(PPh3)3].3H2O (26)
[Ag2(hpda)(PPh3)4].C7H8 (27)
%T
80
70
60
50
85
75
3000
2000
1000
Wavenumbers (cm-1)

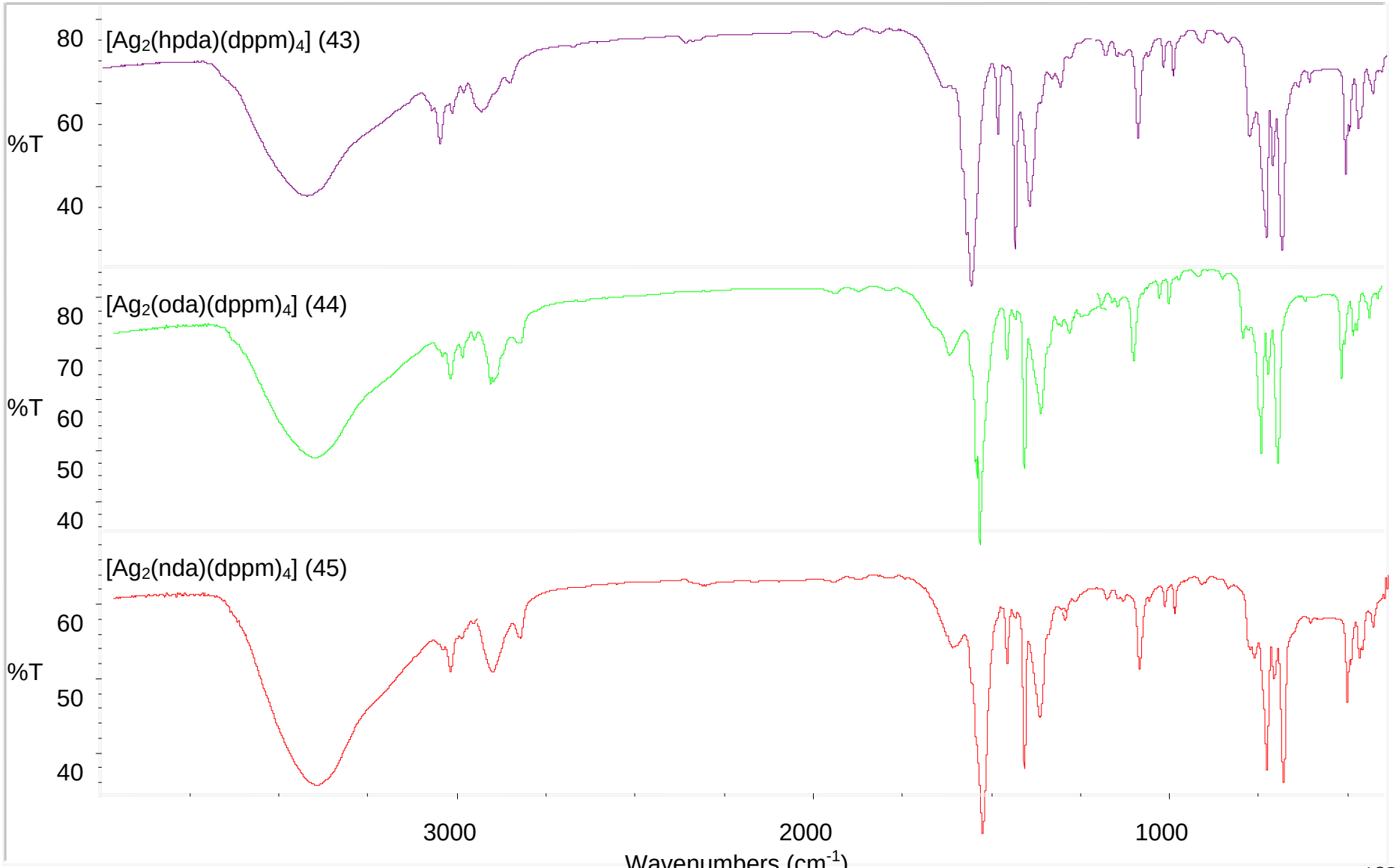

[Ag(odaH)(PPh3)2].C7H8 (28)
%T
60
40
20
[Ag(ndaH)(PPh3)2] (29)
%T
80
70
60
50
40
[Ag2(dda)(PPh3)4].H2O (30)
%T
80
75
70
65
60
3000
2000
1000
Wavenumbers (cm-1)

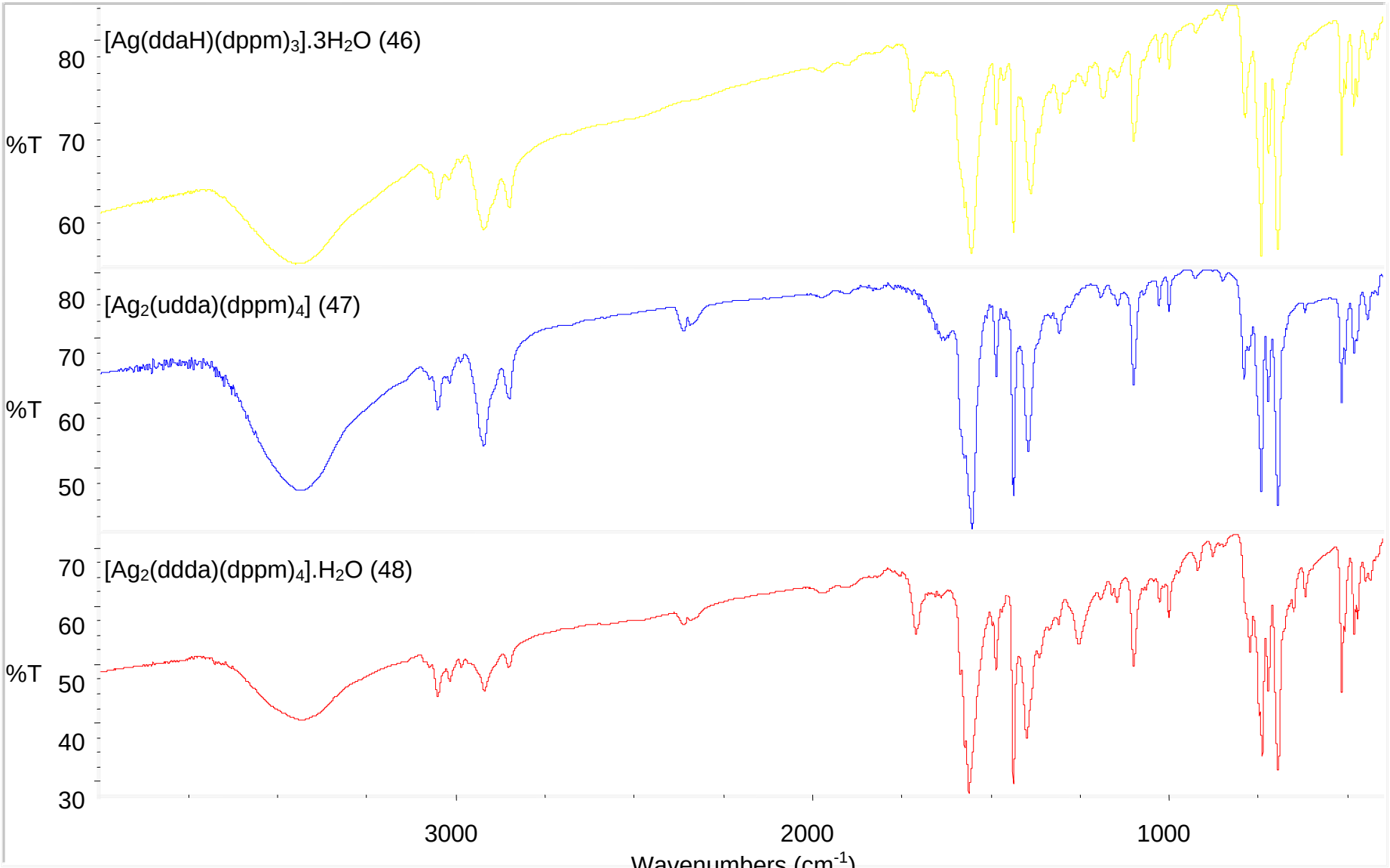

[Ag2(udda)(PPh3)3] (31)
%T
70
60
50
[Ag2(dddaH)(PPh3)3] (32)
%T
40
70
60
50
40
[Ag2(uddcaH)(PPh3)2] (33)
%T
30
80
75
70
65
60
3000
2000
1000
Wavenumbers (cm-1)

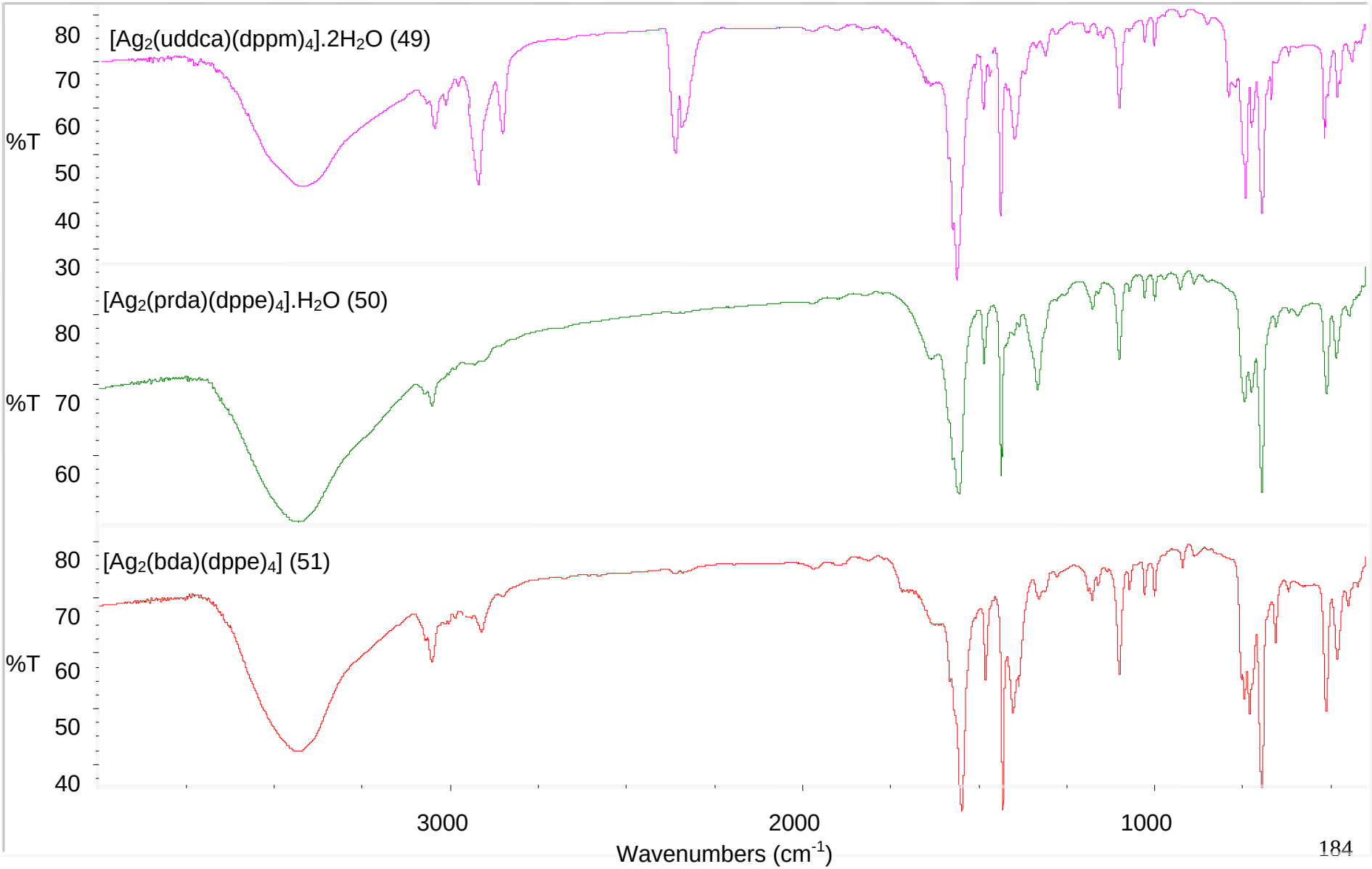

[Ag2(hxdaH)(PPh3)2].C7H8 (34)
[Ag2(hpda)(PPh3)5].C7H8 (35)
[Ag2(oda)(PPh3)4].2C7H8 (36)
%T
80
70
60
50
40
30
85
75
3000
2000
1000
Wavenumbers (cm-1)

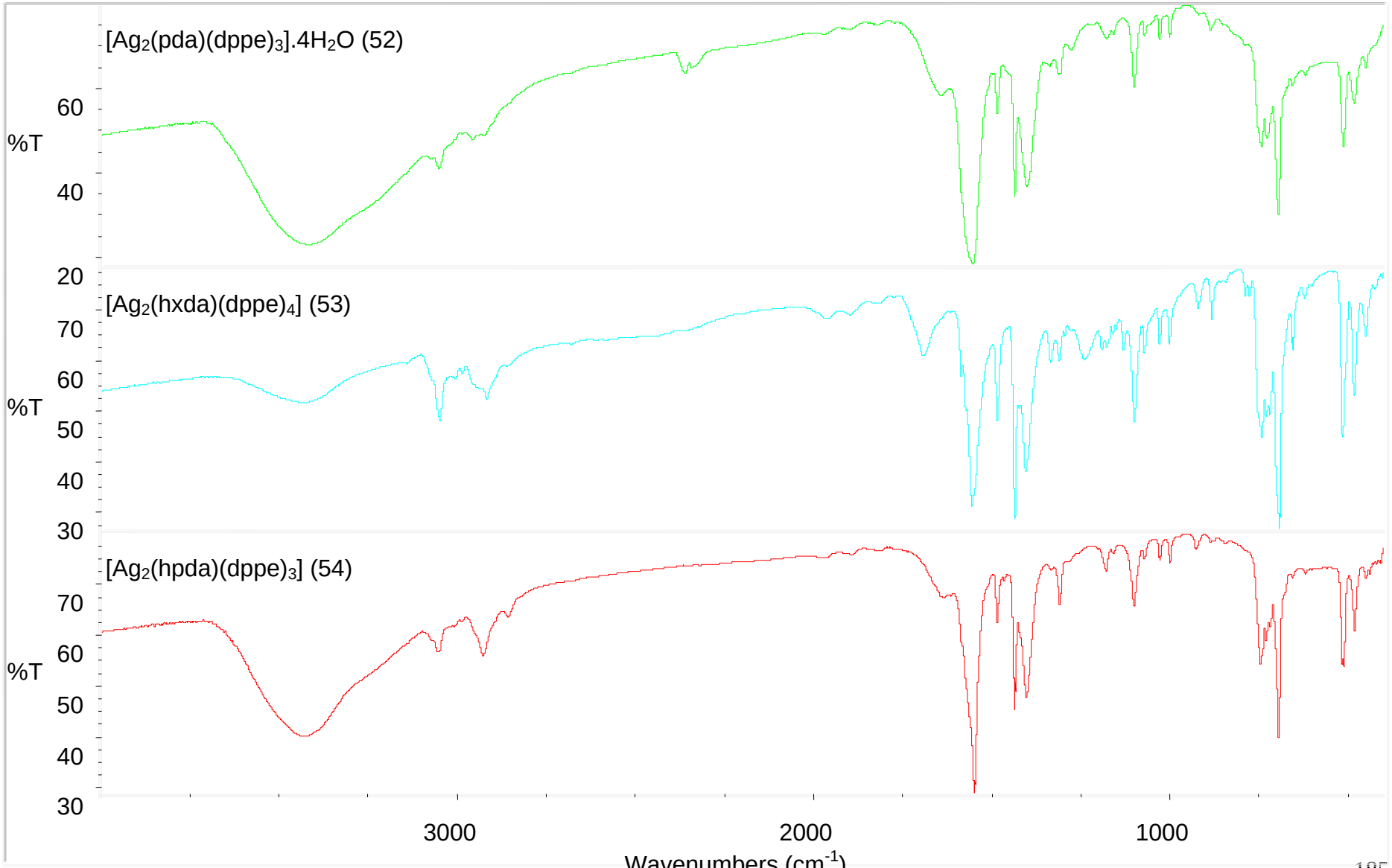

[Ag2(udda)(PPh3)4] (37)
[Ag2(uddca)(PPh3)5].C7H8 (38)
[Ag2(prda)(dppm)3].C7H8 (39)
%T
80
70
60
50
40
20
3000
2000
1000
Wavenumbers (cm-1)

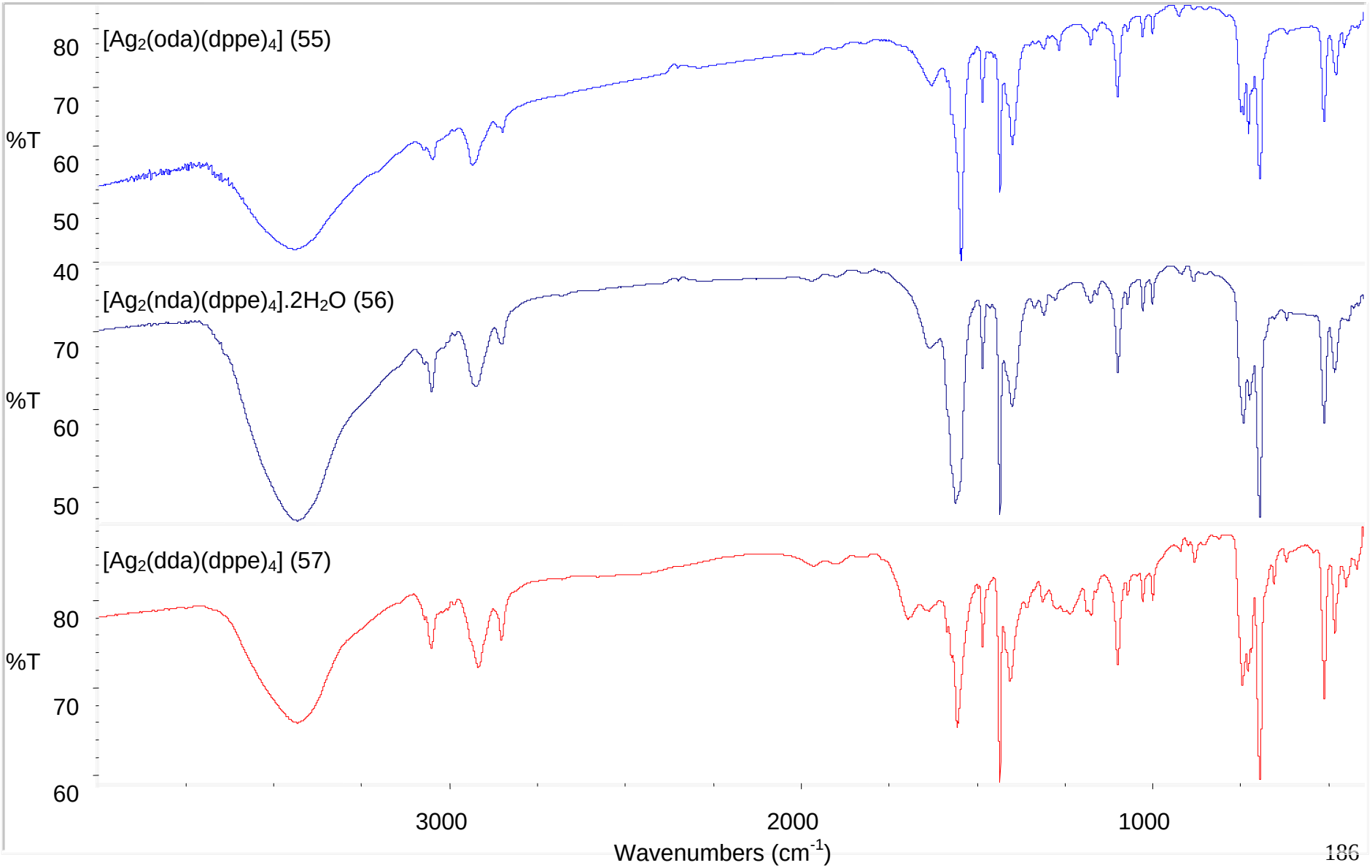

[Ag2(bda)(dppm)3].C7H8 (40)
%T
80
60
40
20
[Ag2(pda)(dppm)4] (41)
%T
80
70
60
[Ag2(hxda)(dppm)4] (42)
%T
70
60
50
40
3000
2000
1000
Wavenumbers (cm-1)

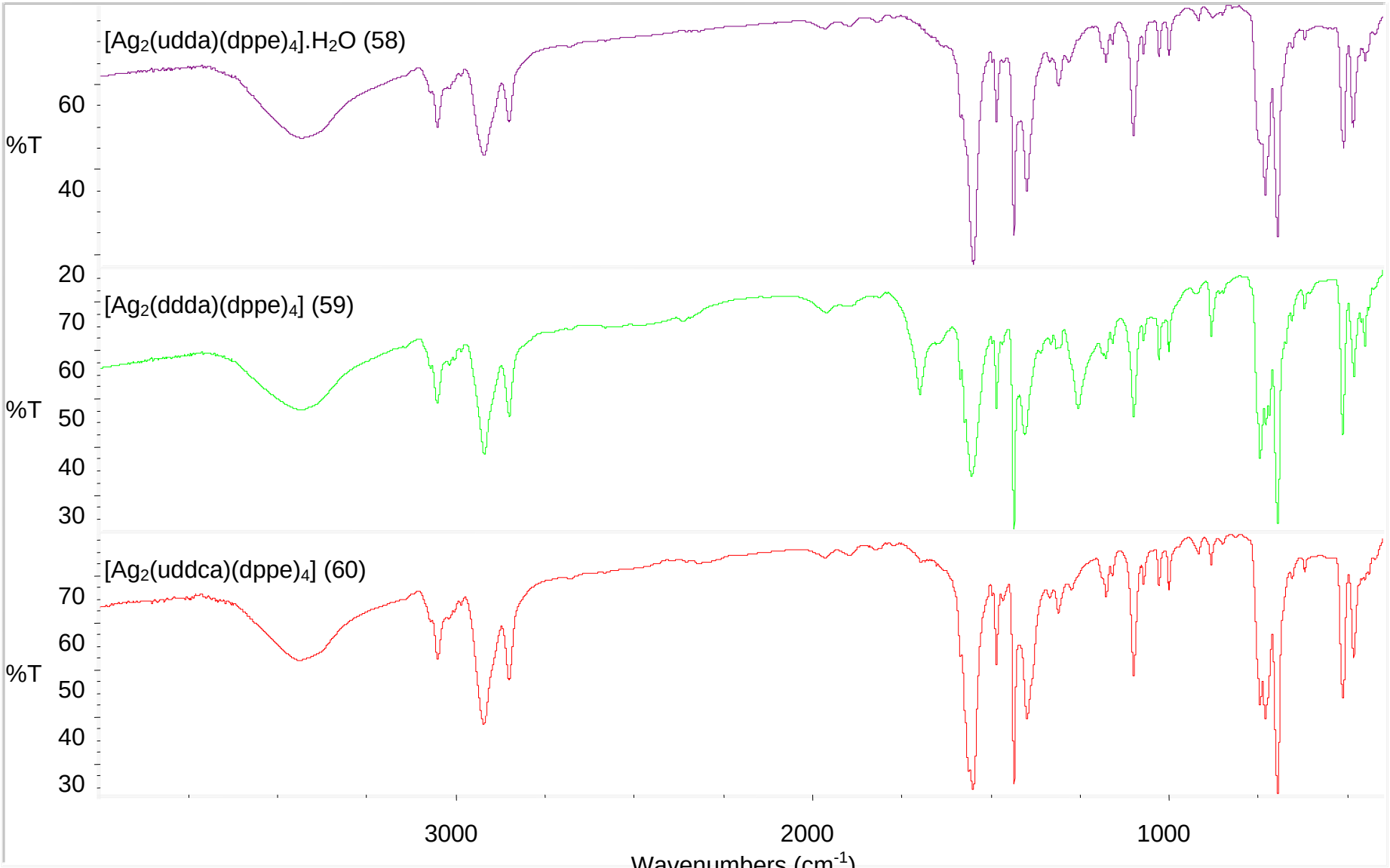

[Ag2(hpda)(dppm)4] (43)
%T
80
60
40
[Ag2(oda)(dppm)4] (44)
%T
80
70
60
50
40
[Ag2(nda)(dppm)4] (45)
%T
60
50
40
3000
2000
1000
Wavenumbers (cm-1)


[Ag(ddaH)(dppm)3].3H2O (46)
[Ag2(udda)(dppm)4] (47)
[Ag2(ddda)(dppm)4].H2O (48)
%T
80
70
60
50
40
30
3000
2000
1000
Wavenumbers (cm-1)


[Ag2(uddca)(dppm)4].2H2O (49)
[Ag2(prda)(dppe)4].H2O (50)
[Ag2(bda)(dppe)4] (51)
%T
80
70
60
50
40
30
3000
2000
1000
Wavenumbers (cm-1)


[Ag2(pda)(dppe)3].4H2O (52)
%T
60
40
[Ag2(hxda)(dppe)4] (53)
%T
20
70
60
50
40
30
[Ag2(hpda)(dppe)3] (54)
%T
70
60
50
40
30
3000
2000
1000
Wavenumbers (cm-1)


[Ag2(oda)(dppe)4] (55)
%T
80
70
60
50
[Ag2(nda)(dppe)4].2H2O (56)
%T
40
70
60
50
[Ag2(dda)(dppe)4] (57)
%T
80
70
60
3000
2000
1000
Wavenumbers (cm-1)


[Ag2(udda)(dppe)4].H2O (58)
%T
60
40
20
[Ag2(ddda)(dppe)4] (59)
%T
70
60
50
40
30
[Ag2(uddca)(dppe)4] (60)
%T
70
60
50
40
30
3000
2000
1000
Wavenumbers (cm-1)